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#### WIDE FIELD ROENTGEN THERAPY

WITH REPORT ON CLINICAL INVESTIGATIONS, 1920–1938\*

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HERE were several reasons why I ▲ chose "Wide Field Roentgen Therapy" as my subject when invited to deliver the Mackenzie-Davidson Lecture at the Annual Congress of the British Institute of Radiology. In the first place the method had been under constant investigation for nearly twenty years and had always been to me a subject of very great interest. Secondly, I consider that it will be in the realm of radiotherapeutics that the greatest advances will be made in the future. Finally, I came to the conclusion that the time was ripe and the occasion appropriate for me to render an account of investigations that were commenced at the London Hospital in 1921 when I was Director of the Radiological Department.

Originally the object of the investigation was to determine whether wide field roent-gen therapy could influence, that is prevent, the formation of secondary deposits in malignant disease especially in carcinoma mammae. It is only in the last eight years that it has become evident that this method of roentgen therapy has a much wider scope when applied to the less spectacular benign conditions.

I realized, as anyone with a wide experience of cancer in general and of carcinoma mammae in particular, must realize only too well, that it is rare for the primary growth to destroy the host. The fact that it is the metastases that do all the killing must be faced. From the earliest history of medicine it has always been the formation of secondary deposits that has rendered abortive the various methods devised from time to time for the destruction of the primary growth, whether this be through the agency of hot irons, surgery, roentgen rays or radium, etc. For this reason I have always maintained that even if total destruction of the primary growth were possible in 100 per cent of cases the effect on the cancer problem would probably be negligible; consequently whether it be roentgen rays produced at one million volts or radium in bulk, that is applied locally for destruction of the primary growth, a cure cannot reasonably be expected.

Until it is generally appreciated also that so-called deep roentgen therapy is not the *only* method of roentgen application and that cancer is not the *only* condition

<sup>\*</sup> Abstract of the Mackenzie-Davidson Memorial Lecture, delivered at the Annual Congress of the British Institute of Radiology, December, 1937.

that can be benefited by roentgen rays but little progress in radiotherapeutics can be hoped for. The radiological departments of all hospitals are at present designed primarily for the treatment of cancer by the "deep roentgen-ray" method, but it is no use hiding the fact any longer that in this disease the ultimate results, from the curative point of view, are disappointing, although the palliative effects may often be spectacular.

In any case it is surely wrong that the energies of a radiological department should be entirely devoted to the treatment of an interesting but rare disease like cancer, to the exclusion of the less spectacular but more prevalent benign conditions which are known to benefit from roentgen irradiation.

The problem therefore in 1920 was to find some method that had a reasonable chance of preventing and destroying metastases. This vital problem has yet to be solved.

Since the beginning of radiotherapy the application of roentgen rays has always been to a limited area, and consequently the biological effect has been limited to this area. Obviously, therefore, this restricted application of roentgen rays cannot be expected to have any influence whatever on preventing the formation of metastases or of destroying secondary deposits which more than likely are scattered throughout the body long before they can be detected clinically. The localized irradiation of the "gland areas" must be equally ineffective. Obviously, therefore, if the power of destroying malignant cells within a localized area was to be extended. to the destruction of these stray or wandering malignant cells, the whole body would have to be submitted to irradiation. The question would then arise whether the dose necessary to accomplish this destruction might not at the same time destroy the host. A certain amount of research work that had some bearing on this problem had been carried out during this period (1921).

The conclusions were as follows:

- (a) A large dose of roentgen rays was found to be detrimental to health and eventually caused death of the animal—while there was an *increased susceptibility* to tumor growth.
- (b) Smaller doses, while detrimental to health, did not endanger life.
- (c) Still smaller doses not only improved health but reduced susceptibility to tumor growth.<sup>1,2,8,4,6,6</sup>

The whole animal was exposed to irradiation. The last of these findings (c) formed the foundation of wide field roentgen therapy.

It must be clearly understood that there is nothing antagonistic between the intensive local application of roentgen rays namely, deep roentgen therapy—and wide field roentgen therapy any more than thereis between surgery and medicine. Each is used for a specific purpose. Deep roentgen therapy which produces a direct local destructive effect might be called surgical radiotherapy; wide field roentgen therapy, on the other hand, as will be shown later, results in an indirect or constitutional effect and for this reason might be termed medical radiotherapy. In cancer both methods are probably necessary, one to destroy the primary growth, the other to prevent the formation of metastases. I purposely refrained from publishing the results of this prophylactic method, although at the London Hospital a large number of cases had been treated over a number of years. The fact that the majority of patients treated belonged to the roving population of the East End of London made it possible to follow up only about I per cent of cases over a period long enough to estimate results. I have no hesitation, however in saying, even in the absence of statistics. that wide field roentgen therapy undoubtedly seems to possess, in a certain percentage of cases, the power of reducing the possibility of the formation of secondary deposits. At any rate there is sufficient evidence to justify some cancer research body continuing this investigation into prophylaxis. This new method of application certainly opens up flew lines of therapy worth investigating on a large scale.

#### HISTORY

Thanks to the generosity of Mr. Serena, at that time a member of the House Committee at the London Hospital -(1921), it became possible to install a specially designed apparatus for this investigation.

The early machine consisted of two roentgen-ray tubes, one in front and the other behind the patient, activated separately but running simultaneously. The tubes were so arranged that at 12 inches the radiation field included the whole trunk, back and front (Fig. 1). The result-

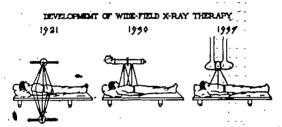


Fig. 1. Development of wide field roentgen therapy.

ing flooding of the tissues, using roentgen rays of long-medium wave length (0.095 Å) made it essential to ascertain whether the patient might not be detrimentally affected and whether he would survive the treatment.

It was about this time that detrimental blood changes, usually a leukopenia, were being reported as occurring among those working with roentgen rays or radium. It was with some trepidation, therefore, that the first cases were submitted to this new method of roentgen application. No record could be found of this method having been tried previously. Several illustrations were, however, found in an old German book on radiology (Fig. 2), suggesting this idea, • but the text made it clear that for technical reasons it was never carried out. If it had been developed, I am sure that radiotherapeutics would by now be in a much more advanced state.

The first 50 cases treated by this method

were closely watched and a careful record of the blood was kept during the first year. Curiously enough, the ultimate report of the pathologist on these cases was essentially favorable; a general improve-

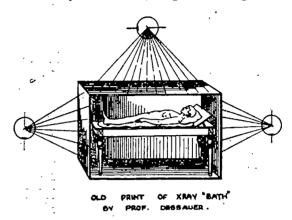


Fig. 2. Old print of roentgen-ray "bath" by Prof. Dessauer.

ment in health and in the blood picture was a constant feature.

This at least meant that no har was being done, but it was not till some ten years later that the real significance of these findings became recognized.

Wide field roentgen therapy now became established at the London Hospital as a routine in all cases of malignant disease, being used *in conjunction* with any local application (deep roentgen therapy) to the primary growth considered necessary.

These investigations were continued up to the time of my retirement from the London Hospital in 1930, after twenty-two years as Director of the Radiological Department. Thanks to the facilities granted by the Charterhouse Rheumatism Clinic, it has been possible to continue the work, but only in relation to benign and rheumatic conditions, it being realized that, owing to the want of facilities, the cancer problem had for the time being to be shelved, hoping that later some cancer research body might carry on the investigations.

Larly in these clinical investigations I realized that further advance in this method of roentgen-ray application was

not to be expected until some tangible test could be found that would register the constitutional change or effect now so clearly demonstrated by the clinical results.

Owing to the practical difficulties, efforts to obtain this evidence from the examination of urine, feces, blood and saliva, etc., at periods before, during and after irradiation proved abortive. The effect on the sedimentation test, however, was found of some value, but unreliable. It was the preliminary work of Bendien that made the introduction of the differential sedimentation test possible. When Dr. Coke, of the Charterhouse Clinic, suggested five years ago (1933) that the method might supply the information I was wanting, I must say that, owing to the complexity and delicacy of the technique, I was very sceptical of its practical value; nevertheless, it was decided to test it out in this research. This test, a serological sedimentation, has now been carried out in a large number of cases treated by wide field roentgen therapy and has enabled this method of treatment to be developed along more scientific and less empirical lines. I have come to compare its use with that of registration of the body temperature. Its actual value lies in the fact that it seems to supply information as to (1) severity of the infection; (2) degree of toxicity; (3) amount of resistance, and this with a considerable degree of accuracy. It also, as will be described later, gives information that is of some assistance in regulating dosage. With wide field roentgen therapy there is a "saturation" point that can be recognized. Dr. Coke states that the differential sedimentation test has shown:

- a) that serological changes can be observed as the result of exposure of X radiation, given by the wide field radiation method in comparatively small doses.
- b) That having apprehended the nature of such change, the test has been applied as a means of controlling dosage and overdosage that is over-saturation.

The investigation so far indicates that

to reach the optimum effect, the patient should be kept as near as possible to the saturation point, over- or under-saturation being avoided. All the skill of a physician is therefore required to estimate the effect of each treatment. Those using deep roentgen therapy will hardly appreciate that the difference between saturation and over-saturation may in some instances be only a matter of 10 r when using wide field roentgen therapy.

Whether the differential sedimentation test will ever become generally established, I do not know; however, these investigations have clearly demonstrated that it possesses a definite value in this method of roentgen treatment and in difficult cases I would not like to be without it, but it should be realized that its use is not essential to the treatment and that good results can be attained if careful attention is paid to the effect of each individual treatment. From the point of view of these investigations, therefore, we have in the differential sedimentation test a means of registering an effect of wide field irradiation on the organism as a whole. This fact has accounted for the advance in technique in recent years.

Let us now consider the fundamental differences between deep and wide field roentgen therapy. It may be said at once that the only thing in common is the use of the same agent. Deep therapy means the use of roentgen rays of very short wave length; thick filters; small radiation field; large doses. The effect is of a destructive nature. The radiation beam is locally applied to some objective sign of disease, such as a tumor, enlarged glands, etc. If the mass so treated disappears, the result is considered satisfactory, ignoring the fact that this mass may be but the manifestation of a constitutional condition. A mass of glands in a case of Hodgkin's disease • is an example. Such a mass may rapidly, disappear under the influence of roentgen rays, but the effect on the disease as a whole is negligible—other glands will eventually develop throughout the body. The

condition, stamina, age, etc., of the patient : does not suggest any adjustment of dose. If he does not survive the treatment, the fault lies with the patient and not with the radiologist! The motto of deep therapy may be said to be "the larger the dose, the better the result." One is rather inclined to think that under these circumstances the patient comes to be looked upon as "something" attached to a tumor! This method of roentgen-ray application may, I think, be described as surgical radiotherapy, and undoubtedly has its dangers and the reaction unfortunately often lowers resistance beyond recovery in the case of an enfeebled patient.

It may be thought that the only feature of this new method of radiotherapy lies in the fact that the rays are applied to a large, instead of a local, body area. This is wrong. The whole principle is different, requiring an entirely new outlook and a readjustment of ideas.

Wide field roentgen therapy entails the use of roentgen rays of medium wave length, light filters, large radiation field (the whole trunk), optimum distance and small doses (comparative). The effect, moreover, is not local but generalized or constitutional. Briefly, one treats the disease through the patient; the patient, in other words, receives all the attention and not the outward manifestation of the disease. These investigations go to show that in some complex way the patient's resistance can be raised, he is thus able to establish an ascendency over whatever pathological condition he may be suffering from, and if the response is satisfactory, the patient will be in a position to cure himself, irrespective of the disease. In other words, if the findings of these investigations are confirmed, then the necessity for treating each disease as a separate entity •will cease—a somewhat revolutionary out-

It must be realized that it is natural to be well and unnatural to be ill, and that illness or ill health is nothing more than evidence of a breakdown in this resistance to disease. Nature is always striving to keep us fit, in the same way that she readily repairs any damage, such as fractured bones, wounds, etc., but she cannot have a separate defense against every disease. Our conception of disease is arbitrary and therefore the names of diseases mean nothing to her. She cannot, for instance, have a special defense for typhoid and another for pneumonia. Her methods of defense must therefore be of the simplest kind. If means could be found of keeping this defensive power up to maximum and of restoring it when for some reason or other it has dropped below normal—that is, a lowering of resistance—an incalculable blessing would be conveyed on mankind. There is fortunately something described by Hernaman-Johnson as "that innate tendency of the body to swing back to the rhythm of health—vis mediacatrix naturae."

It is not improbable that an individual who is born with a high resistance and retains this during life, is the one that reaches a ripe old age.

I have deliberately allowed myself to indulge in what some might call fantasy. with the object of accentuating the fundamental differences between the two methods of roentgen therapy. The principles and objects are so entirely different. I am inclined, therefore, to describe the wide field roentgen application as medical roentgen therapy. In contrast to the surgical, or deep, roentgen therapy, it is the smaller rather than the larger dose that gives the best results. It might be said that with deep roentgen therapy it is the tumor that is treated and with wide field roentgen therapy it is the patient. The introduction of short wave roentgen therapy, with the additional influence of physicists, has led the radiologist to substitute physics for biology; thus he has become more of a technician and less of a physician, a state of affeirs that unfortunately cannot lead to any real advance.

There has always been that tendency to treat the objective sign or signs of disease rather than the disease itself. If a patient has a lump or a pain and this objective sign disappears with treatment, it is often erroneously concluded that he has reaped some real benefit from the treatment, until the objective signs return in some other part of his body, when it is realized that he is suffering from some constitutional condition, the primary cause of the objective signs.

6

In the course of these investigations, this fact has always had to be kept in view and additional evidence of improvement has had therefore to be looked for in directions such as an improvement in the blood picture, sedimentation rate, increase in weight, improvement in appearance of the patient, texture of the skin and, above all, the patient being conscious of a feeling of "well-being"

The trial of this method in a large number of cases, embracing many pathological groups, has definitely shown that no two patient respond exactly alike—that the response is greater in the young patient—that there is no danger or possibility of damage in the application of this method, provided the principles are understood and the technical details followed.

#### THEORY OF ACTION

This research work has made it quite clear, therefore, from clinical results so far obtained that the whole "makeup" of the patient or individual can be influenced by wide field roentgen therapy. How does this come about? What evidence is there to support this contention? What is the evidence that resistance to disease can be raised by this method of roentgen-ray apeplication? Will it ever become possible to register this essential resistance and will means ever be found of keeping it up to a maximum? All pertinent questions. It is humiliating to think that the medical profession can do so little to prevent such complaints as the common cold of influenza. In fact, doctors are unable to show their real worth until it comes to diagnosis or treatment. We want specialists of health as well as of disease. The evidence so far

obtained strongly supports the idea that this power of resistance to disease is in some. complex manner bound up with the uniform functioning of the ductless or secretory gland system as a unit, an imbalance of which may mean a depression of this resistance automatically followed by the risk of disease or ill-health. My contention, which of course requires much research before it can become established, is that wide field roentgen therapy can restore this endocrine balance. The sensitivity of glandular tissue to roentgen rays in diseases of the thyroid, spleen, etc., is already well established, but the possibility of influencing the ductless gland system as a unit with the possibility of preventing disease has not as yet been considered.

Hirsch (1925) points out in his book "The Principles and Practice of Roentgen Therapy" when dealing with this subject of the effect of roentgen rays on secretory gland tissue, "that with proper small doses a stimulation of the secretory function is produced.

"With proper moderate doses inhibitory effects with restitution to normal of the secretory function may be produced.

"With *large* doses the effects of degeneration and death of the particular tissue may be produced.

"The effect of X-rays on the function of a secreting tissue might therefore be expressed as follows: Destructive dose 100%, inhibitive dose 75%-50%; stimulative dose 35-25%."

Of course I do not know on what authority this work is based but these investigations tend to confirm the findings. At any rate, there is here a wast field for the research worker.

It has been suggested that the preservation of a high resistance should prevent or at any nate reduce the possibility of disease but to prove this will require considerable investigation.

The method has been tried out in various pathological conditions. Working on the assumption, rightly or wrongly, that the therapeutic effect of wide field roentgen

therapy is indirect or constitutional, resulting in a raising of resistance, it soon became evident that irrespective of the pathological group to which the case belonged, if a general response to irradiation could be registered, then the patient got well. Thus one found the clinical results, for example, in spondylitis adolescens were equally as good as those obtained in certain types of asthma, Hodgkin's disease, blood diseases, etc., all belonging to different groups. Of course, the response varies in different individuals, but in most cases this can be accounted for by the stage of the disease, debility and age of the patient, rather than by the actual nature of the disease.

Eventually I was forced to the conclusion that the clinical results were dependent on the response that could be obtained in the patient rather than any effect directly on the disease—meaning that the patient rather than the disease was being treated. At first sight this conclusion apbears unreasonable, especially to those engaged in deep roentgen therapy where it is customary for the tumor rather than the patient to receive all the attention. This outlook is not so revolutionary as it appears. Our methods of treating disease are really so limited that in most cases all we can do is to place the patient under conditions that will encourage his recovery, treat his symptoms, and let nature do the rest. Thus medical advice, to go on a cruise, to take a tonic or to have a change at Brighton, are only different methods of treating the patient. Consequently, the time may come when diagnosis will be of minor rather than of major importance, knowing that if a patient feels ill and his resistance by any means can be restored rapidly, his recovery is assured even in the absence of a diagnosis. Of course, this may be considered to be a flight of imagination, but at any rate it helps to accentuate the large gap that exists between the objects of deep and wide field roentgen therapy.

Let us sum up the evidence so far collected during these investigations in support of the contention that the effect of wide field roentgen therapy is of a constitutional character. It is hardly necessary at this stage to stress the importance of this

- (a) improvement in the blood picture,
- (b) the restoration of the blood sedimentation rate to normal,
- (c) the influence on the serum as demonstrated by the differential sedimentation test,
- (d) character of the post-irradiation phenomena,
- (e) effect on general metabolism,
  - (1) increase or decrease in weight,
  - (2) feeling of well-being,
  - (3) an increase in mental alertness,
  - (4) increase in physical fitness,
  - (5) improvement in skin texture.

The effect on the blood is possibly the most significant. The registration of the influence on resistance of this form of irradiation as demonstrated by the differential sedimentation test is of special interest and work is to be continued along these lines.

It follows theoretically that if the resistance is raised to all diseases, it should be possible in certain conditions to get the patient well from several pathological lesions at the same time. This has actually happened in several cases. Thus an antrum full of pus cleared up while treating a patient by wide field roentgen therapy for an active spondylitis. Another patient undergoing this treatment for an inoperable sarcoma in the abdomen was cured of his asthma and was alive and well three years later. Migraine and asthma have also been influenced simultaneously. Other cases could be quoted.

#### TECHNIQUE

Several workers have made use of teleradiotherapy, the distance of the tube to the patient varying from 6 to 24 ft. This, of course, results in a large radiation field, but as I have pointed out the use of a large field alone does not constitute wide field rocate therapy any more than the use of a small field constitutes deep roentgen therapy.

Heublein<sup>8</sup> describes the arrangement of

a ward where the roentgen-ray tube, running automatically day and night, irradiated 5 patients at once over a period of seven days—twenty hours a day—in some cases even up to thirteen days! A canary placed in the primary beam succumbed after receiving 7 erythema doses! He reports some degree of general stimulation of the metabolism of the patients, but arrived at no conclusion.

A glance through the literature on the use of large radiation fields makes it clear that:

- (a) Roentgen rays of short wave length have invariably been used.
- (b) The rays have been passed through a copper filter, creating a homogeneous primary beam.
- (c) The distance of the tube to the patient has never been less than 6 feet.
- (d) The effect has been direct. Even under these conditions favorable results have occasionally been reported.

The essentials of wide field roentgen therapy as used in these investigations may be summed up for comparison, as follows:

- (a) The use of roentgen rays of long-medium wave length.
- (b) The use of light aluminum filters.
- (c) A heterogeneous primary beam.
- (d) A large radiation field—the whole trunk.
- (e) Optimum distance—a maximum of 20 inches—tube to patient.
- (f) The recognition of a saturation or tolerance dose.
- (a) Wave Length. Most of the recent investigations have been carried out with a wave length obtained at 130-140 kv. The new wide-angle roentgen tube which has been installed at the new Charterhouse Rheumatism Clinic where this work is to be continued will run at a constant rating of 100 kv. The object of this new roentgen tube will be described later.

It must be clearly understood that the choice of wave length is dependent on obtaining the maximum body absorption.

Penetration must be adjusted accordingly. I do not propose to become involved in

physics. But the choice of wave length and the number of roentgens administered when using this method must be entirely dependent on the effect produced on the individual, similar to the administration of drugs.

- (b) Filters. The primary use of a filter is to absorb those rays that are not required. With the use of the longer wave lengths, it is the skin that has to be protected. Three millimeters of aluminum has been found quite sufficient when using 130-140 kv., especially as the dose administered to the skin by this method, owing to the different principle of application, is quite one-sixth less than the full unit skin dose. The use of a light filter also tends to give a more heterogeneous primary beam, a quality that would seem to be desirable in achieving the best results. As soon as the new clinic is complete, a comparison is to be made between the biological or stimulating effect of 130 kv. with a filter of 3 mm. Al and that obtained by 100 kv. using a filter of 1 mm. Al.
- (c) Field—the new wide-angle tube. The importance of the size of the radiation field has frequently been stressed, how the employment of a large field does not necessarily mean that wide field roentgen therapy is being used. There are many other factors to be taken into consideration.

Owing to the construction of self-protected tube, there has always been the difficulty in obtaining a large enough field at the optimum distance of tube to patient, 17-20 inches. At this distance the limited opening in the shield only allows of a field of approximately 12 inches in diameter. The average length of the trunk that has to be covered is 22 inches. All the more recent investigations, that is during the last six years, have been carried out with the two field method. This means that the dose has been divided fifty-fifty of er two overlapping field. Unlike short wave roentgen therapy uniform absorption over the whole area is not necessary. It should be realized that here the object of irradiation is only to produce in the patient a certain "state,"

called saturation, which is indicated by certain post-irradiation phenomena. The wide-angle tube has been so designed that at 17 inches it gives a spread of approximately 22 inches. Time in a busy hospital will thus be saved by the use of this tube, a single field supplanting the double. This method of roentgen application is not unlike that used with ultraviolet rays (Fig. 3).

Optimum Distance of Tube to Patient. From actual experience it has been found that working under the conditions here mentioned the biological or constitutional effect on the patient, on which the results depend, diminishes if the tube is farther than 20 inches from the skin, even though the full number of roentgens are, administered. I do not intend to explain this phenomenon.

(d) Dosage. The principles of wide field roentgen therapy are so entirely different from those of short wave therapy that there is really nothing in common, except the use of the same agent, so that comparison is made difficult. I have referred to short wave therapy as surgical radiotherapy and wide field radiation as medical radiotherapy. To emphasize further the difference between the rationale of the two methods, and how dosage is dependent on other factors, I am accustomed to compare the pharmacopeial uses of unguentum arseni and liquor arsenicalis. The ointment may contain a sufficiently large amount of arsenic to destroy the tissues. With the liquor, on the other hand, arsenic is given in minute quantities by mouth and yet this may easily produce signs of poisoning. The objects of treatment, the dose and the type of case treated, are so different in these two methods of drug administration that the use of the same therapeutic agent is the only thing in common. Short wave roentgen therapy may be compared with the use of the ointment, and wide field therapy with the use of the liquor.

I have already mentioned that 60-1∞ r measured in the center of the radiation field represents the average dose required to produce the signs of saturation or of

tolerance which are necessary to obtain results. It is wiser to err on the side of under-rather than of over-saturation. In contradistinction to short wave therapy, it is the smaller dose that gives the more satisfactory results. Investigations have so far shown that 100 r per treatment is about the maximum dose necessary although in

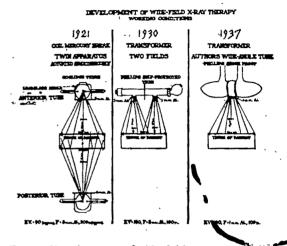


Fig. 3. Development of wide field roentgen therapy, working conditions.

special cases up to 200 r have been tried. Obviously the roentgens administered by this method are of a different therapeutical or biological value from those registered in short wave roentgen therapy. In the same way as the dose of 600-700 r is with deep roentgen therapy called the unit skin dose, u.s.d., so 100 r might be called with wide field radiation the unit body dose—or preferably, the term total body dose, T.B.D. It is of importance that the hospital roentgenographer be instructed to vary the total body dose according to the reaction noticed by the patient after the previous exposure. It is necessary to keep the patient up to saturation point, neither above nor too far below this level. The radiologist must therefore become more of a physician and less of a technician if he is to obtain the best results. The first dose which should not be more than 60 r is given with the idea of astertaining the radiosensitivity of the individual. In difficult cases the differential. sedimentation test has proved, during

these investigations, to be of considerable value in determining whether saturation or over-saturation has been reached. There is a possibility in some cases of increasing the "negative phase" as it is called, instead of developing the necessary "positive phase." Over-saturation can occur without any uncomfortable phenomena being experienced by the patient.

(e) Frequency of Irradiation. The frequency and number of treatments has been found to be dependent on so many factors, such as the type and stage of the disease, age, stamina and debility of the patient, the effect of treatment, etc., that it is not easy to lay down any hard and fast rules.

In one case, for example, the patient is young and there is no time to waste if the condition is to be brought under control, sessions twice weekly for three weeks are then indicated. In another case, we have an elderly woman whose resistance is probably at a low ebb, who will need very careful handling if any benefit is to follow. Here once weekly for six or eight sessions would be advisable. Too frequent irradiation should be avoided.

The object, as far as practicable, is to keep up saturation over a definite period, usually one month. Unless the patient can arrange to attend regularly for a stated period, treatment should be refused or else postponed. Avoid, however, wherever possible the "wait and see" policy, so popular with the patient and his doctor. Procrastination is often disastrous; if it is decided that treatment can be of value, there can be no legitimate reason for delay.

These investigations have clearly shown that once control has been obtained of the pathological condition, this control should be kept up by carefully planned prophylactic measures. See that the patient understands the object and importance of these measures. To postpone further treatment until the disease shows clinical evidence of recurrence is not logical or justifiable.

This has been found to be particularly important in blood and glandular conditions like Hodgkin's disease. This work has indicated that carefully planned prophy-

lactic measures and avoidance of overdosage will keep these patients symptom-free and well for many years longer than is possible with other methods of technique.

Unless the patient is prepared to "stay the course" and be under observation for the stipulated period, treatment of the case should not be undertaken.

- (f) Delayed Action. Patients and the doctors should be warned that the beneficial effect of this method of roentgen. application is often delayed for a month or more after the first course of treatment is completed. The patient usually expects an immediate and miraculous result. This is unreasonable, considering the disease has probably been progressing for months or even years. This delayed action should be explained, especially as the patient usually feels rather worse at first; there is some stir up of symptoms, and possibly some degree of depression, etc. He is then apt to think the treatment is doing no good. He finds it hard to believe that these signs are favorable. Another point should be made clear to the patient, that relief of symptoms is no criterion as to the effects of treatment. In some cases relief of pain is spectacular and the patient erroneously thinking he is cured, ceases to attend, only to appear in due course with a recurrence.
- (g) Gauging of Results. It is not easy to determine whether some particular method of treatment is really influencing the disease as a whole—whether it is having just a palliative effect or in fact whether it is doing any good at all. It is obvious, for instance, that in a condition like asthma the fact that the attacks happen to cease with treatment cannot of itself be proof that the disease is being influenced in the slightest degree. The patient has probably had similar intervals of freedom without any treatment. From the commencement of these investigations, special efforts have been made to find some indication of improvement independent of what the patient may say. So that now, in addition to any relief of symptoms or diminution in objective signs, evidence of improvement is looked for in the weight, general appear-

ance, feeling of well-being, alteration in the sedimentation rate—effect on the differential sedimentation test—blood picture, roentgenological changes, etc.

#### POST-IRRADIATION PHENOMENA AND THE SIGNS OF SATURATION

A number of curious and puzzling phenomena have been noticed during these investigations occurring at different intervals after irradiation. These have been tabulated. Many thousands of cases have now been submitted to this method of roentgen treatment and it is rare for the patient not to mention at least one of these post-irradiation phenomena.

A certain number of these indicate the saturation level. They occur within twelve hours of treatment. Others indicate oversaturation, a condition which is undesirable. The remainder are recorded but their significance is at present unknown. It should be realized that these curious and in many cases bizarre occurrences are quite unexpected by the patient, in fact, it is seldom that they connect them with the treatment. There is no question of suggestion. I am convinced that some day the key to the problem will be found and the explanation of the phenomena will be forthcoming.

The signs of saturation are important to recognize. A curious abdominal sensation, up to slight nausea likened to that of seasickness or pregnancy, is the most common symptom. Then we have giddiness, headache, lassitude and even an uplift as alternatives. An aggravation of symptoms is not uncommon, all usually occurring within twelve hours. The roentgens must be regulated so that none of these signs are excessive—a difference of only 10 r may separate saturation and over-saturation.

To me the most interesting of this list of post-irradiation phenomena is the effect on bowel action. A definite percentage of patients mention a stimulation of bowel action, with others a normal evacuation may become established without aperient. A remark, "I have had a normal action of the bowels, the first for twenty years," is not

unusual. Three actions daily may occur but, curiously enough, this increased bowel activity is never accompanied by a griping or abdominal discomfort. In most cases this improvement is permanent, in others it lasts but a few months. Large evacuations and green stools lasting several weeks have also been recorded. Some abnormality in taste is also very frequent, variously described as metallic, oily or just "nasty." A still more interesting observation is the production of a distinctive if unpleasant body odor for some hours after treatment. The patient complains that this is conveyed not only to their clothes but also to their towel and sponge!

As the effect of the irradiation begins to be felt, a definite alteration in mental efficiency is noted, especially in the young. Backward school children become bright; in one instance a girl while undergoing this method of treatment for asthma, passed from the bottom of the class to the top and obtained a scholarship! This interesting effect is to be further investigated. The changes mentally and physically are often very striking.

Increase in weight in the younger patients is found to be an important sign of improvement. This is often remarkable in asthma and spondylitic cases; an increase of two stone in as many months has often been noted. The record increase was in a case of generalized malignant disease, treated by this method for investigation purposes. The weight had been reduced to 6 stone 13 pounds and the patient moribund when first seen; within eight months this had increased to 12 stone and the patient was well.

I consider that each individual has a healthy weight which will not vary as long as he is in health. A loss or an increase of weight may be the only sign of ill health.

> EFFECT OF WIDE FIELD ROENTGEN THERAPY IN A VARIETY OF PATHO-LOGICAL CONDITIONS

Object. To collect evidence supporting the theory that wide field roentgen therapy creates a constitutional condition, possibly

#### TABLE I

#### POST-IRRADIATION PHENOMENA

The following post-irradiation phenomena have frequently been noted while investigating the effects of this method of treatment, in a large number of different types of cases. The significance of these is at present unknown but apparently they are not detrimental to the patient.

#### Gastrointestinal (temporary)

- (1) Vague abdominal sensation
- (2) Slight nausea
- (3) Flatulence and borborygmi
- (4) Acute hunger
- (5) Thirst
- (6) Hiccough
- (7) Looseness and regulation of bowel action (frequent and in some cases permanent)
- (8) Slight pyrexia
- (9) Vomiting
- (10) Reduction in abdominal distention
- (11) Improvement in digestion (in some cases permanen)

#### 🌓 ervous System (temporary)

- (1) Giddiness
- (2) Headache
- (3) Initability
- (4) Increase of growth of hair on the head
- (5) Nervy
- (6) Curious tingling of extremities
- (7) Flushes
- (8) Depression—apprehension
- (9) Increase of perspiration
- (10) Curious body odor for about twelve hours

#### Senses (temporary)

#### Taste

#### Smell

- (1) Bad
- (1) Distortion and everything smells bad
- (2) Metallic
- (2) Return after loss in asthma
- (3) Coppery
- (3) Disappearance of nasal catarrh (asthmatic)
- (4) Oily
- (5) Salty
- (6) Acid

#### Hearing

- (1) May become very acute for one hour or so
- (2) Noises in head may disappear for several weeks

#### Urogenital (temporary)

- (1) Frequency of micturition.
- (2) Amenorrhea
- (3) Painful uterine contractions
- (4) Aphrodisiac effect

I have included all those phenomena, however fantastic, that have been noticed by more than three patients. Even so, some are no doubt psychological. a raising of resistance, that enables the patient to cure himself irrespective of the disease.

The interest in these investigations was greatly increased when it became suspected that this method of roentgen application did not influence the disease directly, but that any beneficial effect depended on the response of the patient.

It was now realized that it might be possible to control disease, not by treating the outward manifestation but simply by stimulating the patient's resistance. New and fascinating possibilities suggested themselves. Table III gives some idea of the amount and type of clinical work covered, and Table IV what remains to be investigated. Owing to the want of facilities, it has only been possible to concentrate on a few pathological conditions, but the results obtained in various diseases mentioned in Table III have been sufficiently interesting and convincing to call for confirmation by those who have the facilities.

#### TABLE II

#### POST-IRRADIATION PHENOMENA

- (a) Signs of saturation or tolerance dose noticed within 12 hours of treatment.
- (1) Vague abdominal sensations
- (2) Slight nausea
- (3) Definite nausea similar to sea-sickness or morning sickness in pregnancy
- (4) Giddiness
- (5) Headache, frontal
- (6) Lassitude
- (7) Depression and apprehension
- (8) Uplift; feeling of well-being
- (b) Signs of over-saturation (to be avoided).
- (1) Severe nausea
- (2) Vomiting
- (3) Pyrexia
- (4) Loss of weight
- (5) Shift to left with differential sedimentation test
- (6) A rise in sedimentation rate
- (c) Signs of treatment being ineffective.
- (1) Absence of any signs of saturation irrespective of dose
- (2) General deterioration of the patient
- (3) Loss of weight
- (4) Shift to left with differential sedimentation test
- (5) A rise in sedimentation rate

I will briefly give my conclusions on the investigations, extending over some twenty years, into the therapeutic value of the method in a few pathological conditions.

Malignant Disease Group. In cases of cancer mammae, originally devised as a prophylactic measure (1920), wide field roentgen therapy has produced results which, even in the absence of reliable statistics, justify further investigation by some cancer research body.

The few cases of general dissemination such as carcinomatosis, multiple secondary deposits, myelomatosis that have been investigated, have shown remarkable effects, indicating that this method has a very considerable palliative value, provided over-saturation is avoided.

Allergic Group. Asthma, from a chance observation in 1922, was the first benign condition found to respond to this method. Considerable research work in this condition has been possible during the last few years. I have come to the conclusion, after treating a large number of these cases, that there can be no question that in the uncomplicated allergic type the results are so satisfactory and certain that the method must eventually come to be established as a routine treatment measure. It has already been introduced with success in several hospitals. On the technical side these investigations have shown that the results are more satisfactory if the thorax is entirely eliminated from the radiation field. Oer-saturation must also be carefully avoided.

Rheumatism Group. Investigations into the effect of wide field roentgen therapy on this group have extended over a period of six years. I am convinced it must prove of definite value in certain varieties of chronic generalized rheumatism. However, for various reasons, it was decided to limit the investigation to one type, namely the ankylosing spondylitis or spondylitis adolescens, the spinal arthritis that attacks young adults, usually an athlete in his rime. Four hundred patients have been investigated clinically and roentgengraphi-

cally. It is necessary to mention the final conclusions as being of some importance. The onset of this disease can now be detected clinically and roentgenographically five to seven years before the onset of spinal pain and stiffness: (a) clinically, by recurrent attacks in early life of rheumatic pain in the limbs, joints, thorax and abdomen, but not in the back or sacroiliac joints; (b) roentgenographically, by progressive pathological changes in the sacroiliac joints (sacroilioitis) during this period.

It has been shown that if wide field roentgen therapy is used during the prespondylitic period, that is before the spine is involved, there is no reason why this tragic disease should not be wiped out. This conclusion is based on results, many of which have been remarkable, noted while investigating the effects of the method in about 200 cases. This is by far the most important practical result that has yet emanated from these investigations; they are being continued.

This disease is not rare but it is not being recognized or treated in its early stages. Whenever a healthy youngster complains that he is "rheumatic," always suspect changes in the sacroiliac joints, now known to be associated with an early spondylitis.

Rheumatoid Arthritis. A few cases have been investigated of this type of arthritis which should theoretically respond to this method of roentgen application. The results certainly tend to confirm this. Given facilities, this is the next piece of work to be carried out.

Diseases of the Blood and Lymphatic Glands. Investigation in this group has shown that life can be prolonged and the patient will remain symptom-free nearly four times as long when wide field therapy is used as with any local method of roentgen-ray application. Over-saturation should be avoided as well as too frequent irradiation. An occasional dose as a prophylactic measure is essential even in the absence of symptoms.

The majority of diseases mentioned in

#### TABLE III

DISEASE GROUPS SO FAR INVESTIGATED BY WIDE FIELD ROENTGEN THERAPY. 1920-1938

- xxx Over 100 cases treated.
- xx Under 100 cases treated.
  - Under 12 cases treated.

#### Allergic Group

xxx Asthma

- x Urticaria
- x Migraine

#### Endocrine or Metabolic Group

Backward children

#### Lymphatic Gland Group

- Hodgkin's disease, lymphadenoma and allied conditions
  - Lymphosarcoma

#### Blood Group

- xx Leukemin (typical and atypical)
- Polycyt lemia

#### Neuroses Group (? Endocrine Imbalance)

- Functional or the neurotic X
- Phobias X
- Menopausal Х
- x Functional backache
- x General debility

#### Rheumatic Group

- x Spondylitis osteo-arthritica
- Spondylitis adolescens or ankylosing spondylitis
- Rheumatoid arthritis X
- xx Fibrositis
- Rheumatic backache—lumbago
- Polyarthritis and periarticular rheumatism

#### Chronic Infective Group

- Osteomyelitis
- Chronic septic conditions

#### Skin Group

- x
- Psoriasis Multiple warts x
  - Fibromata x
  - Generalized eczema and furunculosis
  - Alopecia

#### Malignant Disease Group

xxx Prophylactic

- x Carcinomatosis
- x Myelomatosis

Tables III and IV are definitely outside the scope of deep roentgen therapy. This fact alone must make it clear that an entirely new field in radiotherapeutics is opened up. Needless to say, much of this work needs confirmation by others. However, these investigations have produced sufficient evidence to support our original contention and at least indicate the lines along which work should continue.

So few cases have been investigated in the other groups mentioned in Table III that no conclusions are possible. These tables should be studied by those anxious to prove that it is possible to influence disease through altering the patient's makeup.

#### TABLE IV

CASES NOT YET INVESTIGATED, BUT THEORETICALLY SHOULD RESPOND

#### Endocrine or Metabolic Group

Abnormal loss or increase of weight without cause especially in children Abnormal growth or defective development of children (not congenital)

#### Blood Group

Hemophilia Leukopenia Certain anemias

Neurosis Group Mental defectives Enuresis

#### Acute Infective Group (Generalized)

Pyemia Septicemia

Ductless Gland Group

Diabetes Hyperthyroidism Hypothyroidism

Deficiency Diseases

Rickets Osteomalacia

#### SUMMARY

- (1) A description is given of the development of a method of roentgen-ray application called wide field roentgen therapy.
- (2) Investigations extending over a period of some twenty years into the value of this method in a variety of pathological conditions are outlined.
- (3) It is pointed out how the principle of the method is entirely different from

that of short wave or deep roentgen ther. apy.

- (4) It is shown how irradiation of the whole trunk by roentgen rays of low intensity in small doses produces constitutional rather than local effects.
- (5) The result would appear to be a raising of the general resistance to disease, comparable to the effects of ultraviolet, or sunlight, only a hundredfold more effective.
- (6) A theory as to how this effect is being obtained is put forward.
- (7) In order to appreciate the gap that exists between the two methods, deep therapy is denoted as *surgical* radiotherapy; wide field radiation as *medical* radiotherapy.
- (8) The method was originally designed as a prophylactic measure in malignant diseases.
- (9) Results obtained in large numbers of cases clearly indicate that work in this direction should be continued by some cancer research body.
- (10) Certain blood tests—the sedimentation rate and the newer differential sedimentation test—have enabled the constitutional effect of irradiation on the patient to be recorded. This has led to a rapid development during the last six years in the treatment of pathological conditions other than cancer.
- (11) This method of roentgen-ray application has been tried out, on a limited scale, in many diseases with very interesting results.
- (12) These results indicated that they were being obtained through some general influence on the patient rather than through any direct effect on the objective signs of the disease.
- (13) Investigations now show that it is possible to influence pathological conditions hitherto quite outside the scope of short wave roentgen therapy or in fact any form of local applications of roentgen rays.
- (14) Owing to the want of facilities and funds, investigation into the value of this method has had to be limited. The material being available, chronic rheumatic condi-

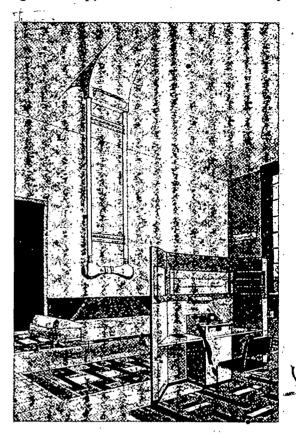


Fig. 4. Drawing of wide field roentgen therapy department at the Charterhouse Clinic, showing the wide-angle roentgen tube.

tions, ankylosing spondylitis and asthma have been mainly dealt with. The first practical result of this investigation is that a serious rheumatic condition, known as ankylosing spondylitis or spondylitis adolescens, will eventually be eradicated.

- (15) The center for this research work has of late years been at the Charterhouse Rheumatism Clinic, London.
- (16) For technical reasons, a new wideangle roentgen tube has been designed by Philips, for this method of roentgen-ray application.
- (17) It enables the whole trunk to be irradiated at the optimum distance of tube to patient of 20 inches. This tube, is to be installed at the new Charterhouse Rheumatism Clinic where this work is to be continued (Fig. 4).
- (18) The technique is described and how the signs of saturation or tolerance can be

recognized by certain post-irradiation phenomena.

- (19) A list of remarkable as yet unexplained post-irradiation phenomena is given.
- (20) The beneficial effects on the patient with wide field roentgen therapy as registered by the blood, weight, general health and the improvement mentally and physically are discussed.
- (21) Owing to the smallness of the dose administered, 60-100 r, there are no dangers or possibilities of damage to the patient as long as the rules of technique are adhered to.
- (22) A report is given with conclusions on the various investigations that have been carried out in the last twenty years into the influence of wide field roentgen therapy on disease generally. Tables of diseases are given.
- (23) It is stressed that this work is far from complete, but it is felt that a report should now be published so that other workers may be stimulated to give the method a trial.
- (24) The place that this therapeutic method takes in medicine must in the

future be entirely dependent on the clinical results obtained.

#### REFERENCES

- ULLMANN, H. J. Radiation dosage: standardization versus individual adaptation. Radiology, 1923, 1, 31-33.
- 2. Russ, S., Chambers, H., and Scott, G. On local and generalised action of radium and x-rays upon tumour growth. *Arch. Radiol. & Electroth*, 1921, 26, 129.
- 3. Murphy, J. B., and Morton, J. J. The lymphocyte as a factor in natural and induced resistance to transplanted cancer. II. Studies in lymphoid activity. J. Exper. Med., 1915, 22, 204-211.
- 4. MOTTRAM, J. C., and Russ, S. Observations and experiments on the susceptibility and immunity of rats towards Jensen's rat sarcoma. *Proc. Roy. Soc.*, Lond., Ser. B., 1917–1918, 90, 1–33.
- 5. PRIME, F. Lymphocytes and cancer immunity. J. Cancer Research, 1920, 5, 105.
- MURPHY, J. B., and NAKAHARA, W. Studies on x-ray effects, biological action of small doses of low frequency x-rays. J. Exper. Med., 1922, 35, 475–486.
- Charterhouse Rheumatism Clinic. Origina papers, 1937.
- 8. Heublein, A. C. Preliminary report on continuous irradiation of entire body. *Radiology*, 1932, 18, 1051-1062.



#### THE COMBINED ROENTGEN AND RADIUM TREAT-MENT OF CARCINOMA OF THE CERVIX\*

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In 1937, we reported the results of combined roentgen-ray and radium treatment in 70 cases of carcinoma of the cervix. These cases were irradiated at the Pondville Hospital at Norfolk (Massachusetts Department of Public Health) and were followed for three and a half years after treatment. All patients showing evidence of disease at the end of this period were classified as dead. The cases were chosen without selection, the only prerequisites being that there should have been no previous irradiation and no operative procedure.

The method of irradiation employed was as follows: Roentgen rays generated at 200 kv. with a filtration of 0.5 mm. of copper were applied at a distance of 50 cm. to each of four pelvic portals, two anterior oblique and two posterior oblique. The size of these portals was either 8 by 10 cm. or 10 by 10 cm. Distances greater than 50 cm. were employed in a few cases, but it was felt that the depth dose was not sufficiently increased to warrant the extra expenditure of energy. Furthermore, experiments with filters heavier than 0.5 mm. of copper showed no clinical increase in skin tolerance, and there was only a 2 per cent increase in the 10 cm. depth dose. The results of these experiments with filtration are now in press.1

Daily treatments of from 300 to 600 r (200 measurement) were employed, alternating the fields so that a given area was exposed every fourth day. Each field received a maximum of 1,500 to 2,000 r, the total dosage depending upon the rapidity with which the treatment was given and the general feaction of the patient. In most instances daily exposures of 400 r were administered, the series being completed

within three weeks. A few days following the roentgen therapy, heavily filtered radium was applied within the uterine canal, two doses of 1,500 millicurie- (milligram) hours being given four days apart. In all instances, a biopsy was taken before the roentgen therapy, after completion of the roentgen series, and after the first radium application. There was no con-

TABLE I

	Total	3½ Year	Percent-
	Cases	Survival	age
Roentgen rays and radium	70	. 25	35.7
Radium alone	150	38	25.4
Surgery alone		23	38.3

sistency in the grading of the tumors, and frequently all three grades of carcinoma were found in the same tumor at different stages of treatment. Those tumors which after the roentgen treatment showed microscopically "radium reaction only" gave the best results. It is believed that the biopsy following the completion of the roentgen series may prove of considerable prognostic value.

For comparison with this series of 70 cases treated by the method of combined roentgen and radium irradiation, a series of 150 cases treated by radium alone, and also 60 cases operated on without irradiation were reviewed. The three and a half year results are shown in Table 1. It will be noted that the 35 per cent salvage by combined roentgen and radium treatment is 10 per cent better than that obtained by radium alone, and nearly equals the results in the small selected group subjected to hysterectomy.

<sup>\*</sup> Read at the Thirty-Ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N.I., Sept. 20-23, 1938.

A classification according to the stage of the disease is shown in Table II. Although the radium dose was smaller when combined with roentgen irradiation than that employed when radium alone was used, the figures show a 100 per cent survival of the A and B cases. This indicates that sufficient radiation was delivered by the combined method to satisfactorily control disease limited to the cervix or in close proximity to the cervix.

Because of the rapid falling off of intensity by the inverse square law, the amount of radiation delivered at a distance cancer of the cervix do so within the first three and a half years, and that for statistical purposes it is not essential to wait for five year results.

During the winter of 1936, a machine became available at the Collis P. Huntington Memorial Hospital for supervoltage roentgen therapy. This apparatus was designed and built by the High Voltage Research Group at the Massachusetts Institute of Technology, and has been fully described in previous communications.<sup>3 4 6</sup>

Fifty-nine cases of carcinoma of the cervix have thus far recevied supervoltage

TABLE II

	A	В	c	D
Roentgen rays and radium	5	3	45	17
Radium alone	15	13	100	22
Surgery a one	28	11	20	I
- ' [	3½ Yea	r Survival		
Roentge rays and radium	5100.%	3-100%	16-35.5%	1-5.8%
Radium alone	12- 80%	7-53.8%	18—18%	
Surgery alone	13-46.4%		5-25%	_

of 1.5 to 2 cm. by 3,000 mc-hr. of radium is hardly sufficient to control epidermoid carcinoma. Therefore, we cannot expect to be successful in combating disease which has extended beyond the cervix by the use of an intrauterine applicator alone. The intravaginal application of radium may be helpful in these cases, but is often technically difficult. The use of roentgen rays externally will augment the radium dose in the peripheral portions of the pelvis, and theoretically should result in a cure of a greater percentage of the more advanced cases. The improved results in the B and c groups obtained by the combined method as compared with radium treatment alone substantiate this theory. The D cases thus far have proved hopeless from every therapeutic standpoint.

The three and a half year results reported in the original communication have recently been brought to five years with only a 2 per cent difference in the total salvage. This would indicate that most of the patients who die after irradiation of

treatment. Approximately half of this number (28) had been treated previously with lower voltage roentgen rays or radium, and were given supervoltage radiation as a palliative measure without hope of cure.

In 31 cases without previous irradiation, a plan of therapy analogous to that used in the Pondville group was carried out. Although the supervoltage dosage was kept reasonably uniform in this group, the radium dosage was varied from 3,000 to 4,000 mc-hr. In many instances, an intravaginal application of radium was made in addition to the intrauterine treatment. The roentgen apparatus was operated t 1,000,000 volts constant potential, with a focal skin distance of 70 cm., and filtration equivalent to 4 to 6 mm. of lead; halfvalue layer of copper 10 to 11 mm. In a. few instances the radium treatment was given before the roentgen treatment, but in the majority of cases the roentgen therapy preceded the radium.

The combined supervoltage and radium

treatment of carcinoma of the cervix has been in use for only eighteen months, and sufficient time has not elapsed for the accumulation of statistical data. However, certain differences between this type of therapy and that employing 200 kv. rays have become apparent. These differences may be classified under skin reaction, effect on the general condition of the patient, reaction of the deep-lying normal structures, and effect on the tumor.

The practice of expressing roentgen dosage in terms of roentgens measured in air has given rise to some confusion. It should be kept in mind that the amount of radiation which the skin receives consists not only of the primary beam, but is augmented by rays which reach the surface through back-scattering. There is a marked difference in the back-scattering from rays produced at 200 kv. as compared with those generated at 1,000 kv. If 10 by 10 cm. fields are employed, about 30 per cent of the skin dosage is derived from ack-scatter with 200 kv. rays, and only 10 per cent of the skin dose is due to backscatter with 1,000 kv. rays. It has been stated that the majority of patients treated at 200 kv. received 400 r per day, air measurement, through 10 by 10 cm. portals. Each of four fields, two anterior oblique and two posterior oblique, was treated with this dosage on consecutive days until each field had received a total of 2,000 r; that is, the entire skin dosage administered on completion of the series was 8,000 r, air measurement. However, if the amount of radiation due to backscatter is added, disregarding the exit dose which is small at 200 kv., the daily dose Fer portal becomes approximately 570 r, and the total dose per portal is approximately 2,850 r. The aggregate skin dose, measured with back-scatter and including • all four portals, amounts to about 11,400 r.

Most of the patients thus irradiated developed severe erythemas, and a larger dosage was not considered safe because of the skin reaction. At one time discrepancies were noted in the severity of the skin re-

actions, which were attributed to variations in the output of the roentgen apparatus due to fluctuations in the line voltage. When this condition was remedied, the skin reactions became more uniform.

Those patients irradiated on the 1,000ooo volt unit were treated through three portals, measuring either 10 by 10 cm. or 12 by 12 cm., one directly anterior above the symphysis and two posterior oblique. The daily dose per portal, measured in air, was 400 r, and a total of 2,000 r was given to each portal. The total dose administered to the skin, including the three portals, was  $6,\infty$  r. If one includes the back-scatter, the daily dose per portal is approximately 440 r at 1,000,000 volts, as compared with 570 r at 200 kv. This makes the total skin dose with back-scatter 2,240 r per portal on the supervoltage unit, as compared with about 2,850 r per portal on the 200 kv. unit. At the conclusion of the series, the patients irradiated on the supervoltage unit received a superficial dose of approximately 6,700 r to the skin, as compared with 11,400 r on the 200 kv. unit.

The tolerance of the skin to 1,000,000 volt roentgen rays as compared with 200 kv. rays is approximately double when comparative ionization measurements are made in air. This discrepancy becomes less when measurements are made on the patients' skin or on the surface of a phantom, but there is still a pronounced difference in favor of the shorter wave lengths. A few of the patients irradiated on the supervoltage unit, using the technique which has been outlined, have shown faint reactions over the posterior oblique areas, but most of them have shown no reaction at all. Over the anterior area, however, a moderately severe erythema almost always develops, which may be attributed chiefly to the exit dose. This dose has been measured on a large group of patients and has been found to average 25 per cent of the intensity delivered initially to each portal on the opposite side of the pelvis. In other words, the anterior area receives 50 per

cent more radiation than either of the posterior oblique areas. In no case has this reaction caused the patient any great discomfort, and the erythemas have all disappeared with the usual subsequent tanning and epilation. The portals of entry have been so planned that the erythema develops anteriorly rather than posteriorly where a reaction, particularly between the gluteal folds, may occasion severe discomfort.

Supervoltage radiation has been tolerated rather better than that administered at lower potentials. Many patients in the 200 kv. group suffered from roentgen sickness. Although roentgen sickness has by no means been absent in those patients treated at the higher voltage, it has been definitely less frequent and less severe. There is a logical explanation for this. There seem to be a relationship between roentgen si kness and the volume of tissue irradiated. We are less likely to have generalized reactions when small portals of entry are used than when large fields are treated. It has already been pointed out that the scattering from the shorter wave length beam is much less than from the longer wave lengths. Because of the diminished scattering, the amount of tissue irradiated on the supervoltage unit is limited more closely by the size of the portal of entry than is the case at lower voltage.

The inhalation of ozone also plays a rôle in the production of generalized roentgen reaction. The supervoltage treatment room is completely separated from the compartment in which the voltage is generated. Moreover, ventilation is obtained by drawing fresh air from outside the building. The presence of ozone is in this manner completely eliminated.

Because of the lessening of roentgen sickness, it is possible to treat many cases on the million volt unit as out-patients, who otherwise would have to be hospitalized.

Routine blood counts have been carried out at the beginning and end of the radia-

tion series. Those patients who are anemic at the outset are likely to do badly nomatter what type of radiation is given. However, when small portals are used, we have noticed no greater untoward effect on the blood from the supervoltage rays than we have from the lower voltage rays. It has rarely been necessary to discontinue treatment because of a fall in the white blood count.

It is perhaps unnecessary to mention that in expressing depth dose in roentgens we deal in percentages of the dose measured at the surface with back-stattering and not with measurements made free in air. We have carried out comparative studies between 200 kv. depth doses and 1,000 kv. depth doses, measurements being made not only in the phantom, but also on cases under routine treatment for carcinoma of the cervix with the ionization chamber in the vagina. In the average female pelvis approximately one-third of the surface dose reaches the region of the cervix with 200 kv. radiation, and about 50 per cent of the surface dose is delivered at 1,000,000 volts. With the method of radiation which we have described, the cervix receives an average dose of 190 r per day when irradiated at 200 kv., and approximately 220 r per day at 1,000,000 volts. The total tumor dose delivered in the lower voltage series was about 3,800 r. As already stated, treatments were given to each of four portals on consecutive days, usually including Sunday, so that the entire series was completed in twenty days. In the higher voltage group, daily doses were given to each of three portals, instead of four portals, and the total tumor dose averaged about 3,300 r. Treatments were not given on Sunday in the latter group and it therefore took seventeen days to complete the series. Thus, at 1,000,000 volts we have delivered a turnor dose some • 400 to 500 r less than the dose administered at 200 kv., and in a slightly shorter period.

In the lower voltage group, no deepseated reactions such as diarrhea and vesical irritation developed as a result of the

roentgen treatment. The total amount of roentgen radiation delivered was limited only by the skin reaction. On the other hand, the supervoltage group has shown a different response. Most of the patients have developed diarrhea toward the end of the series, and many have had tenesmus with frequency and urgency of urination. A few have passed small amounts of blood in the stool. These sequelae are not always present, for in a number of instances the patients have had no complaint whatsoever, and in an occasional case constipation rather than diarrhea has been noted. In supervoltage treatment such as we have employed, it is apparent that we can no longer be guided by the tolerance of the superficial tissues, but must determine the amount of radiation which can safely be given by the reaction in the deeper structures of the pelvis. This is particularly true when small multiple portals of entry are employed. It is well established that increasing-the size of the portal of entry increases the depth dose of 200 kv. radiation, but the depth dose at the higher voltage is much less affected by the size of the field. It is important that the fields irradiated be large enough to include all of the disease-bearing area, but we believe it is bad technique to use excessively large portals merely to increase the depth dose.

It is difficult to explain the appearance of deep-seated reactions in the pelvic cases treated by supervoltage radiation. To be sure, the daily tumor dose has been slightly greater than that administered at 200 kv., but the total dose has been somewhat smaller. The slight difference in time element does not offer a satisfactory solution. It is possible that the thimble chamber does not give us an accurate intensity measurement of the shorter wave lengths, and that we are in fact administering larger doses than our ionization measurements indicate.

A difference in hological reaction may be advanced as another hypothesis. In support of this, we have some experimental data. Work done in collaboration with Dr. John C. Larkin, Resident in Radiology at the Peter Bent Brigham Hospital, Boston, has shown that *Drosophila* eggs placed at various depths in a phantom are more readily killed by 1,000,000 volt rays than by 200 kv. rays.

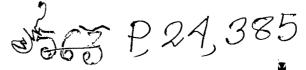
The 31 cases which received supervoltage radiation are classed in Table III according to the stage of the disease. The follow-up period is too short to afford any statistical value. There have been more

TABLE III

	No. of Cases	Immediate Regression
A	ΤΙ	10-90%
В	5	10—90% 4—80%
c	12	975%
D	3	1-33%

favorable cases in the later series than in the group irradiated at the Pondville Hospital.

Satisfactory regression of the disease has been observed in all but one of the Group A cases. This patient, aged sixty-four, was first seen in September, 1937, at which time the cervix was enlarged and involved in a fibrous type of new growth. There was no extension to the vaginal walls, and the body of the uterus was freely movable. No masses could be felt by rectum. The uterocervical segment was broad and edematous. The first biopsy was reported as adenocarcinoma. The patient was given supervoltage radiation during October, and received additional moderate roentgen treatment during November. The second biopsy at the time of radium treatment in December was reported as epidermoid carcinoma, Grade 3. Clinically, the growth had shown considerable though not complete regression from roentgen treatment alone. The patient died outside the hospital about six weeks after the application of radium. Death, as reported by the city clerk, was due to carcinomatosis. Further details are not known. This patient received rather more than the usual amount of roentgen therapy, and the radium dose



was somewhat in excess of 3,000 mc-hr. It seems unlikely that a patient whose local condition was so satisfactory at the time of radium application should have a sufficiently rapid extension of malignant disease to cause death within six weeks. A complicating factor in this case was the presence of diabetes. It is not improbable that this patient's death was not the result of malignancy, but due to the advent of infection, to excessive irradiation, or to a combination of both.

Another patient in the A group received supervoltage therapy without radium. All clinical evidence of disease had disappeared six weeks after completion of the irradiation series, and a month later a complete hysterectomy was performed. Microscopic examination of the cervix after removal showed persistent Grade 2 epidermoid carcinoma. This substantiates our belief that the dosage thus far administered by supervoltage roentgen rays alone is not sufficient to permanently control deep-seated carcinoma.<sup>2</sup>

Of the Group B cases, 4 have done well. The fifth was reported on August 6, 1938, as dying. This patient was thirty-seven years of age, and in October, 1937, showed an enlarged cervix involved throughout with an irregular new growth. There was extension to the vaginal wall on the left side. The uterocervical segment was large and edematous, but quite movable. The patient's general condition was not good. The biopsy report was epidermoid carcinoma, Grade 2. The growth showed little, if any, regression following the supervoltage series given in November, and through some misunderstanding the patient did not receive radium treatment until the latter part of January, at which time it was felt that the case was beyond salvage.

In the c group, 9 cases have shown satisfactory immediate regression. One is dead, another is doing badly and will probably die, and the third patient, irradiated in June, has not returned for follow-up examination.

One of the 3 Group D cases is dead. A second case, recently treated, showed com-

plete softening of both broad ligaments and disappearance of the vaginal wall ex-. tensions following supervoltage radiation. A month after radium treatment there was no palpable evidence of active disease. The third Group D case was considered too far advanced for irradiation of any kind, and it was only on the insistence of the patient's husband that supervoltage therapy was instituted. The response to roentgen treatment was so satisfactory that radium was subsequently given. The pelvic symptoms returned about seven months after irradiation, and the disease again became active. This patient is receiving further roentgen therapy.

#### DISCUSSION

The combined roentgen and radium treatment of carcinoma of the cervix is not presented as a new method. This regimen has been used by other workers in the field of cancer therapy to good advantage. The results observed at the end of three and a half years are encouraging, and these have remained practically unchanged at the end of a five year follow-up period.

Whether or not supervoltage radiation will improve our end-results, we are not at present in a position to say. There are, however, several immediate advantages to be ascribed to the higher voltage therapy. When multiple small portals are employed, the total depth dose which cap be delivered at 200 kv. is limited by the reaction of the skin rather than by any untoward effect on the deeper structures. The reverse is true with 1,000,000 volt therapy. The physiological depth dose obtained from the shorter wave lengths is greater than that measured by the thim ionization chamber, and symptoms of rectal and bladder irritation, which were lacking in the 200 kv. group, have developed in the 1,000 kv. group. The pa-. tients have tolerated the supervoltage treatment rather better than the  $2\infty$  kv. radiation as far as roentgen sickness is concerned.

It is our belief that the dosage thus far administered to the center of the pelvis by

external roentgen irradiation alone is not sufficiently large to permanently control epidermoid carcinoma. With one possible exception, we are not aware of having produced any serious radiation damage with the supervoltage unit. The possibility, however, of late untoward radiation changes looms ever before us, and we therefore feel that great caution must be observed in increasing the dosage. We think that larger amounts of supervoltage radiation than we have thus far administered will eventually be given with safety.

Radium is most likely to fail when parametrial extension of carcinoma of the cervix has occurred. In such cases, it might be well to place our chief reliance on heavy external irradiation, augmented by a small radium dose. On the other hand, in those cases where the disease is limited to the cervix, or has extended slightly beyond the cervix, a modification of technique consisting of a relatively large dose of radium and less roentgen therapy seems logical. Radium has proved so efficacious in the reatment of carcinoma of the cervix that in the present stage of development of our technique of external irradiation we do not feel justified in discarding it entirely.

#### REFERENCES

1. Dresser, R., and Meltzer, A. Effect of heavy filtration on skin tolerance and depth dose. Am. L Roentgenol. & Rad. Therapy, Nov., 1939, 2, 756–759.

2. DRESSER, R., and RUDE, J. C. Supervoltage roentgen treatment of carcinoma of the bladder. J. Am. M. Ass., 1938, 111, 1834-1837.

- 3. Dresser, R., and Spencer, J. Physical and clinical observations on the use of million-volt x-rays. New England J. Med., 1938, 218, 415-
- 4. Dresser, R., Trump, J., and Van de Graaff, R. J. Production of supervoltage roentgen rays by means of an electrostatic generator. Am. J. ROENTGENOL. & RAD. THERAPY, 1937, 38, 758-

5. Meigs, J. V., ap Dresser, R. Carcinoma of the cervix treated by the roentgen ray and radium. Ann. Su g., 1937, 100, 653-667.

6. TRUMP, J. G. and VAN DE GRAAFF, R. J. Design of a million-volt x-ray generator for cancer treatment and research. J. Applied Physics, 1937, 8, 602-606.

#### DISCUSSION

DR. WILLIAM P. HEALY, New York City. I would like to commend the reader of the paper and his associates upon their conservative attitude. This is just a report of progress on their part, and in a general way it verifies what has been done-for a great many years throughout the country and elsewhere in the use of combined radiation methods of therapy for cancer of the cervix.

For about eighteen years, I have been carrying out combined methods of radiation therapy for cancer of the cervix at the Memorial Hospital through the cooperation of the roentgenray department. At first low voltage roentgen therapy, always preceding the radium, was used, but since 1926, we have used high voltage, the 200 kv. During most of that time until about four years ago, we used only four portals, two anterior and two posterior, as has been done by these authors. But for the past four years, we have increased the number of portals

Another point which might be discussed is that with the supervoltage, as utilized by Dr. Dresser and his associates, they have employed one anterior field, the suprapubic field, and two oblique posterior fields, with the anterior field perpendicular. That was done undoubtedly so as to concentrate the rays, the central beam, upon the cervical field, but nevertheless it does concentrate it also upon the rectum and the bladder, and this must result in vesical and rectal irritation, both primary and secondary. The primary symptoms clear up rather quickly but the secondary symptoms may be very unfortunate. These patients may a year or longer after this supervoltage therapy, with the fields set up so that they cross-fire on the rectum and the bladder, have very serious bladder or rectal radiation lesions.

I believe that the plan which we are following at the Memorial Hospital is superior, in which we set up the four to six fields so they are perpendicular to the surface of the body; the beam is perpendicular and goes directly to the parametrium. We want the parametrial field and not the cervix irradiated by the roentgen rays. We plan to take care of the cervical field, the primary lesion, with radium. By setting up the fields perpendicularly, you avoid damaging the bladder and the rectum to the same degree that will occur when you set them up obliquely. We formerly did set up ours obliquely but because

of the sharp proctitis and cystitis which resulted in so many cases, we have omitted doing that.

Dr. Dresser stated that in their cases they apply the radium one week after the termination of the roentgen therapy. We believe that is too soon. Actually, they have not yet obtained in the irradiated fields the full radiation reaction that they are going to get in the tumorbearing area from the roentgen therapy that has been delivered. When they then apply radium on top of it, their patients are much more apt to have severe rectal reactions, rectal ulcers or bladder reactions, than they will have if the application of radium is delayed until approximately three or four weeks after the termination of the roentgen therapy.

Those are very important points for the patient's protection and they do not interfere with the salvage in taking care of the disease. We also believe that roentgen therapy should always be given first. I cannot agree with Dr. Dresser that three and a half years is enough time to dipend on and that thereafter the cases that are well at three and a half will remain well for five. His series, as he says, was quite small in number; five and three in one group and only one or two out would ruin it. He must wait at least five years and then he will find, even after

five years, they will keep falling off from disease, from cancer.

The plan we follow is roentgen irradiation first and then two to four weeks later, radium. Our present method of roentgen irradiation is the pyramidal dose method. We begin with 100 r to each of two opposite fields daily, using six fields. It take three days to go around the pelvis. Then the next cycle is at 150 r and the third cycle is at 200 r to each of two opposite fields; the fourth at 250 r; the fifth at 300 r; the sixth at 350 r, to each of two opposite fields; and the seventh at 350 r. It takes about twenty-one days and at the end of that time the patient has received 1,700 r to each of the six fields with a 200 kv. machine, 70 cm. target-skin distance, and we believe the 70 cm. is better than the 50 cm. They stand it remarkably well. During that time, all these treatments are given with the beam perpendicular, not oblique. Nevertheless, since the cervical field and the tumor field in the cervix is taken in tangentially with the anteroposterior and the posteroanterior treatments, and directly with the lateral treatments, you can see the cervical lesion disappear so that at the end of three weeks, you will have comparatively little primary lesion still evident in the cervix. Then you must wait, as I said, two to four weeks before applying radium.



### THE ROENTGEN DIAGNOSIS AND THERAPY OF RETROPHÄRYNGEAL ADENITIS\*

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RETROPHARYNGEAL adenitis and abscess are fairly common conditions, occurring most often during the first year of life and rarely after the age of three. The roentgen diagnosis of an abscess is easy in most instances, as pointed out by Pancoast and Pendergrass,4 but adenitis or early abscess is often difficult to diagnose because of the normal variations in the size of the retropharyngeal space caused by respiration. Hay studied lateral roentgenograms of the pharynx at rest in 25 normal children varying in ages from three weeks to fourteen years. Because of the difficulty in obtaining roentgenograms of the pharvnx at rest in the uncooperative child, we have adopted a simple procedure for examining and differentiating between the normal and the widened retropharyngeal space. We have reviewed a series of lateral roentgenograms of the nasopharynx in 80 infants from birth to three years of age and our purpose is to present both the normal and the pathological findings.

#### ANATOMY

The retropharyngeal space lies anterior tothe vertebral column and extends upward to the base of the skull. Its downward extension, the retro-esophageal space, communicates with the postpericardial mediastinum. This space contains a network of loose areolar tissue so that in the cadaver the pharynx and esophagus may be easily separated from the prevertebral fascia. It is enclosed anteriorly and posteriorly by two layers of fascia which blend laterally with the sheaths of the great vessels. There is a chain of medial and lateral lymph nodes in the repropharyngeal space. In early life the number of nodes may vary from three to ten but in adult life there are rarely more than one of two as the medial nodes undergo atrophy. The retropharyngeal nodes are the

lymphatic drainage areas for the nasal accessory sinuses, the nasal fossae, the pharynx, the larynx and the middle ear. An initial infection arising in any of these regions may be transmitted through the lymphatics to the retropharyngeal space and extend on downward to the peribronchial nodes or posterior mediastinum. The faucial tonsils have no direct connection with the retropharynx, but drain directly into the deep cervical glands.3 The efferent lymphatics from the retropharyngeal lymph nodes may also drain into the deep cervical glands adjacent to the internal jugular vein, so that glands palpable along the horder of the sternomastoid muscle may receive their infection from either the tonsils or the masal accessory sinuses and nasopharynx.

#### CLINICAL CONSIDERATIONS

A retropharyngeal abscess usually develops from suppuration and breaking down of the retropharyngeal lymph nodes which have become involved due to an infection in the upper respiratory system. The occasional exceptions to this mode of origin are those cases wherein a foreign body has punctured the retropharyngeal or retro-esophageal space. If an infant or child has difficulty in breathing or nursing following an upper respiratory infection, a retropharyngeal swelling with its primary focus in the sinuses, ears or adenoids, as well as an enlarged thymus or pulmonary pathology, must be considered.

#### ROENTGEN DIAGNOSIS

Since the observations on enlarged thymus by Pancoast and Pendergrass,<sup>4</sup> we have included a lateral view of the nasopharynx and chest as a part of the thymus examination in infants. Our routine examination of the sinuses includes a lateral view of the nasopharynx to exclude a retro-

<sup>\*</sup> From the Radiological Clinic of Drs. Groover, Christie and Merritt.

TABLE I

THE NORMAL RETROPHARYNGEAL AND RETROTRACHEAL SPACE

Exposure during Inspiration		28-48 inch Target-Film Distance				
Age	Under 1 year		I to 2 years		2 to 3 years	
No. of cases 40		0				
	Retro- pharyngeal	Retro- tracheal	Retro- pharyngeal	Retro- tracheal	Retro- pharyngeal	Retro- tracheal
Extremes Average	11-3 mm. 7 mm.	18-8 mm. 10 mm.	11-4 mm. 8 mm.	16-8 mm. 11 mm.	11-3 mm. 8 mm.	14-8 mm. 10 mm.

pharyngeal swelling. Because the normal retropharyngeal space varies greatly with the phase of respiration, we exclude this variable factor by making all lateral examinations of the pharynx, neck and chest during inspiration, and to stop motion the time factor is never more than 1/20 and often 1/40 of a second. We have reviewed a series of lateral roentgenograms of 80 apparently healthy children during inspiration to determine the width of the retropharyngeal and retrotracheal spaces. The film target distance has varied from 28 to 48 inches. Measurements were made from the body of the second cervical vertebra to the adjacent posterior pharyngeal wall for the retropharynx. The retrotracheal measurements were made from the posterior tracheal wall just below the larynx to the nearest adjacent vertebral body. The results of these measurements are shown in Table 1.

The normal retropharyngeal space in infants and young children never measures over 11 mm. during inspiration using ordinary roentgenographic distances. The retrotracheal space varies somewhat with age, measuring not over 18 mm. up to one year, not over 16 mm. from one to two years and not over 14 mm. after the age of two. If the pharyngeal air space measures less than 15 mm. it should be suspected that the roentgenograms have not been taken during inspiration and the patient should be re-examined. With very large retropharyngeal swellings the pharyngeal

air space may be partially obliterated even during inspiration, but this is usually easily recognized, as the tongue is pushed forward.

In the past two years we have diagnosed retropharyngeal adenitis in 20 children. It was impossible in a few cases to differentiate between a cellulitis and an adenitis. There have also been 3 cases of retropharyngeal abscess with definite fluctuation on digital examination. These 3 cases offered no difficulty in diagnosis and are not considered in this report, as once suppuration begins the problem is entirely surgical. Table II shows the clinical diagnosis and age in these 20 cases.

As shown in Table II the clinical diagnosis in 6 cases was a nasopharyngitis or sinus disease. Not only did these 6 cases

TABLE II
CLINICAL DIAGNOSIS IN 20 CASES OF
RETROPHARYNGEAL WIDENING

Diagnosis	No. of cases	Age
Nasopharyngitis or sinus disease	6	8 mo. 16 mo. 18 mo. 18 mo. 19 mo. 24 mo.
Enlarged thymus	5	4 wk. 5 wk. 6 wk. 3 mo. 12 mo.
Otitis media	4	7 mo. 9 mo. 10 mo. 20 mc
Foreign body Unexplained fever Cervical adenitis	2 I 2	14 mo. 19 mo. 19 mo. 2½ yr. 3 yr.

have roentgen evidence of sinus disease but all 20 cases showed the antra or ethmoid sinuses to be entirely opaque or have a marked thickening of the lining mucosa. We are impressed with the frequency with which a nasopharyngitis in infants and children is followed by a sinus infection, and occasionally a retropharyngeal adenitis or cellulitis.

In 5 cases the clinical impression was enlarged thymus, because of the age of the patients, the difficulty in breathing and the attacks of cyanosis. The roentgen examination showed the thymus to be normal in size, both in the anteroposterior and lateral views, and the symptoms were due entirely to a retropharyngeal or retrotracheal swelling. On digital examination there was no evidence of fluctuation or abscess. Wasson<sup>6</sup> has shown that the antra are well developed at birth, but are not aerated, and require from four to eight weeks to aerate and become visible on the roentgenogram. In 3 of the 5 cases, aged four, five and six weeks, if we did not have the clinical evidence of a nasopharyngitis with pus in the nose, we could not assume that the opaque antra were diseased.

#### ROENTGEN THERAPY

Roentgen therapy has long been considered a very effective method of treatment for simple cervical adenitis and most radiologists have had experiences similar to Murwitz and Zuckerman.2 They report a carefully studied series of cases with controls showing that suppuration occurred in 14 per cent of cases treated with roentgen therapy in contrast to 41 per cent without roentgen therapy. Inasmuch as have had excellent results with roentgen therapy in chronic sinus disease in children, and finding sinus disease associated so frequently with retropharyngeal swelling, we have recommended small doses of roentgen radiation for all cases of retropharyngeal adenitis, and for all cases of retropharyngeal swelling where there is doubt as to the actual presence of fluctuation.

Of the 20 cases studied all but 3 were treated with roentgen therapy. One case, aged ten months, with a purulent bilateral otitis media and sinus disease, was treated with sulfanilimide and the glands promptly regressed as well as the otitis media and sinusitis. Two cases, aged eight and sixteen months, following a nasopharyngitis had small retropharyngeal glands which caused no obstructive symptoms, and were discovered only by roentgenographing the sinuses. The adenitis and sinus disease disappeared in three weeks following local treatment to the nose.

The remaining 17 cases were treated with roentgen therapy. Since the retropharyngeal adenitis was secondary to an infection in the sinuses or ears, the roentgen treatment was a slight modification of our routine roentgen therapy for sinus disease.<sup>5</sup>

Using 125 kv. (peak), 5 ma, 12 inch distance and 5 mm. aluminum filter, the daily dose is 75 r (measured in air) for infants up to one year, and 100 r (measured in air) from one to five years. One of three 15×15 cm. areas (right lateral, left lateral and anterior) is treated every other day until each area has been treated twice, or a total of six treatments in two weeks. Cases with considerable respiratory difficulty are usually given the two lateral treatments the first day, to hasten resolution. Large areas are used so that the sinuses, the mastoids, the retropharyngeal space and the entire upper respiratory tract is treated. The eyes are protected with small oval lead shields held in place with a band of adhesive tape across the nose. The hair is protected with lead. The uncooperative. child is wrapped securely in a sheet, and the head is held by a nurse who wears heavy lead rubber gloves.

The retropharyngeal swelling disappeared entirely in all 17 cases following the roentgen therapy. The obstructive symptoms usually disappeared after the second treatment. The retropharyngeal swelling did not entirely disappear in any case under two weeks, and in 3 cases it was two

months before the retropharyngeal space returned to normal. We feel that the prompt resolution of the glands without going on to suppuration in any of the cases was due in part to treating the primary focus for the infection as well as the glands themselves.

#### CASE REPORTS

CASE I. Baby E. T., first seen on September 14, 1937, aged six weeks. The baby's delivery was normal and it was perfectly well during ten days' hospitalization. Two days after going home the baby began to cry a great deal and the mother noticed considerable nasal mucus. When fourteen days old the baby began having difficulty in nursing and since then had been unable to breath through its nose. After four weeks of age when the baby was placed over the mother's shoulder with the head partly flexed to regurgitate after feeding, the baby would struggle for air, turn blue and occasionally stop breathing. The baby would be fairly comfortable and breathing was slightly labored when lying on its back with its head flat. An enlarged thymus was suspected and the baby was sent in to the roentgen department for examination of the thymus. Roentgen examination showed the heart, thymus and lungs to be normal. The lateral view of the chest and nasopharynx during inspiration showed the retropharvngeal space to be greatly widened, measuring 15.0 mm. The nasopharynx was blocked. There was also a retrotracheal swelling with compression of the tracheal lumen so that it measured only-1.5 mm. (Fig. 1A). Examination . of the sinuses showed the right antrum to be clear, the left was entirely opaque. Roentgen therapy was advised. Six treatments of 75 r were given and because of the pronounced symptoms, the baby was given 75 r to each lateral area the first day. Following the first day's treatment the baby began to breathe and nurse much easier. A checkup roentgenogram six days later (Fig. 1B) showed the retropharyngeal swelling to be less and the tracheal compression had disappeared. Two weeks after the first treatment the baby was having no symptoms, was breathing through his nose and had gained 14 ounces. The final roentgen checkup, six weeks after roentgen therapy (Fig. 1C) showed the nasopharynx to be normal and the baby has had no further respiratory difficulty.

Case II. Baby D. J., aged two and a half, was first seen on April 17, 1936, complaining of an unexplained fever of three weeks' duration. His temperature would go to 102° F. each day, then following a sudden sweat would drop to normal. Two days before we saw the patient, he developed a small chain of right cervical glands. These glands were given two roentgen treatments of 100 r in three days. The glands promptly disappeared and the temperature remained normal for seven days, when the glands and fever returned. Sinus disease was suspected as the focus for the infection and roentgenograms showed the ethmoid sinuses to be clouded and the antra showed marked

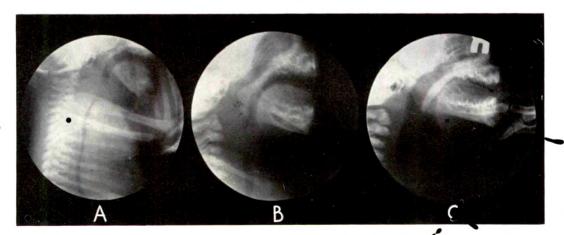


Fig. 1. Case 1. A, the pronounced retropharyngeal and retrotracheal swelling produces almost complete tracheal compression in a six weeks' old infant. B, six days after beginning roentgen therapy the swelling is regressing and the tracheal compression has disappeared. C, six weeks after therapy the retropharyngeal space is normal.

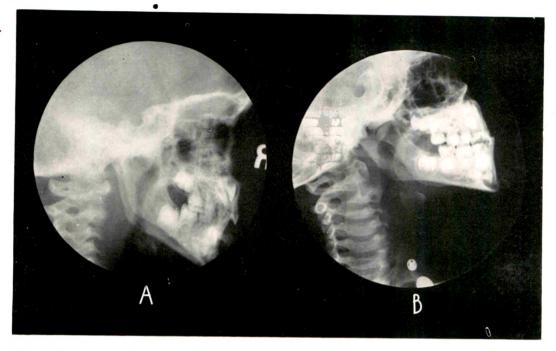


Fig. 2. Case II. A, moderate retropharyngeal adenitis, associated with cervical adenitis and sinusitis. B, one month after roentgen therapy the retropharyngeal space is normal.

thickening of the mucosa. The lateral view of the nasopharynx showed a moderate retropharyngeal swelling which produced no symptoms (Fig. 2A). The patient was given two treatments of 150 r to a large area over the sinuses and pharynx. The large recurrent cervical glands softened, suppurated and were incised and drained. The patient improved immediately. Checkup roentgenogram of the sinuses one month later showed the retropharyngeal space to be normal and the sinuses entirely clear (Fig. 2B).

#### SUMMARY

- 1. The normal retropharyngeal space during inspiration in infants and children should not measure over 11 mm. using winary roentgenographic distances.
- 2. A retropharyngeal swelling is usually due to some focal infection in the upper respiratory tract, often the nasal accessory sinuses.
  - 3. If both the focal infection and the

retropharyngeal swelling, usually an adenitis in the early stages, are treated promptly with roentgen therapy, a retropharyngeal abscess rarely develops.

#### REFERENCES

- 1. Hay, P. D., Jr. The Neck. Ann. Roentgenol., Vol. 9. P. B. Hoeber, Inc., New York, 1930.
- 2. Hurwitz, S., and Zuckerman, S. N. Roentgen rays in treatment of acute cervical adenitis. *J. Pediat.*, 1937, 10, 772-780.
- 3. IGLAUER, S. The Cyclopedia of Medicine. F. A. Davis Co., Philadelphia, 1934, 9, 828-835.
- 4. Pancoast, H. K., and Pendergrass, E. P. Roentgenologic diagnosis of diseases of the upper respiratory tract in children. Am. J. Roentgenol. & Rad. Therapy, 1930, 23, 241-264.
- 5. Rathbone, R. R. Roentgen therapy of chronic sinusitis in children. Am. J. Roentgenol. & Rad. Therapy, 1937, 38, 102–108.
- Wasson, W. W. Changes in nasal accessory sinuses after birth. Arch. Otolaryng., 1933. 17, 197-211.



## ROENTGEN DIAGNOSIS OF DERMOID CYSTS OF THE OVARY IN THE ABSENCE OF CALCIFICATION\*

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THE roentgen diagnosis of dermoid L cysts of the ovary<sup>1-13</sup> is usually based on the presence of teeth or other calcified shadows; the latter may be either amorphous agglomerations or the true osseous formations.3 In many instances the discovery of these tumors is made fortuitously in the course of roentgen studies which include the pelvic abdomen. The incidence of calcification in dermoid cysts is reported in two pathological studies5,8 as varying between 18 and 49 per cent. Since dermoid cysts constitute nearly 20 per cent of all ovarian tumors, it would be desirable to have additional reliable roentgen diagnostic criteria to make possible the detection of the large number of these tumors which do not contain calcareous material.

In the following 6 instances, representative of a group of 22 cases, the roentgen diagnosis of dermoid cyst of the ovary was made on the basis of signs which we believe are constant features of these tumors and which do not depend on the presence of calcified material. A rounded or ovoid mass of decreased density, regular in its contour, is found in the pelvis; it usually presents a banded, mottled appearance. This mass is sharply delineated from the surrounding soft tissues by a thin ring of increased density. Repeated examinations of the same region will always present a similar picture, so that the constancy of these features represents confirmatory evidence.

#### CASE REPORTS

Case I. (Fig. 1A.) J. F., aged twenty-nine. Uterosalpingography was performed because

of a complaint of sterility; the films showed the uterus to be normal. On the left side of the pelvis, in the region of the ovary, a small, rounded area of diminished density was noted. This area was sharply circumscribed by a dense ring shadow, and the mass presented a slightly mottled appearance. The film taken after the lipiodol emptied from the uterus (Fig. 1B) showed the same appearance. The diagnosis of dermoid cyst of the ovary was confirmed at operation.

CASE II. M. H., aged twenty-six. A flat plate of the abdomen, taken for gastrointestinal complaints, revealed in the pelvis a large round mass, measuring about 14 cm. in diameter. The mass presented a banded, mottled appearance and was encircled by a dense ring shadow. No calcified foci could be demonstrated (Fig. 2). On the basis of these features, a diagnosis of dermoid cyst was made and later confirmed at operation. Pathological examination showed no evidence of calcareous material.

CASE III. B. M., aged twenty-three. Studies for urinary complaints included a flat film of the pelvic region and demonstrated a small, irregular calcified shadow in the pelvic region. This shadow, however, was noted to lie within an area of decreased density which was slightly mottled in appearance and encircled by a well defined ring of greater density (Fig. 3). In view of these findings, it was felt that the calcified body represented an imperfect tooth formation within a dermoid cyst. The diagnosis was proved to be correct at operation. This case demonstrates an example where the aforementioned characteristics peculiar to dermoid cyst aided in the differential diagnosis of a calcified shadow in the pelvis.

Case IV. B. G., aged seventy. Roentgen studies of the lumbar spine were made because

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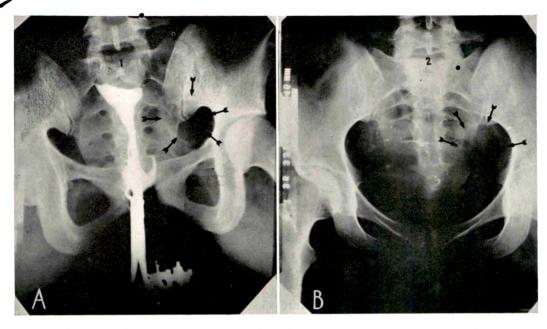


Fig. 1. A, note the relation of the mass to the lipiodol-filled uterus; the latter appears to be normal. The diminished density of the mass is well illustrated. B, the small scattered dense areas are due to small amounts of lipiodol in the pelvis which have gone through the Fallopian tubes. A small residue of lipiodol may also be present within the uterus.

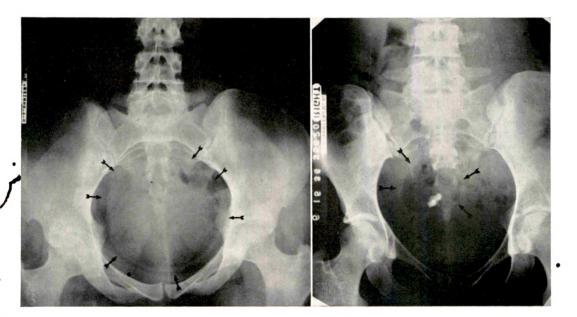


Fig. 2 (left). The encircling ring of the cyst is well defined at the inferior and lateral borders of the mass. This cyst measured 14×11.5×9.5 cm. and contained hair and sebaceous material.
 Fig. 3 (right). The calcified area is poorly differentiated, but was identified as a tooth on pathological examination.

of low back pain. A large, rounded mass was noted in the pelvis; its general appearance was similar to that of the dermoid cysts described

above. The marked degree of mottling was an outstanding feature in this particular instance. An irregular, calcified area was noted in the

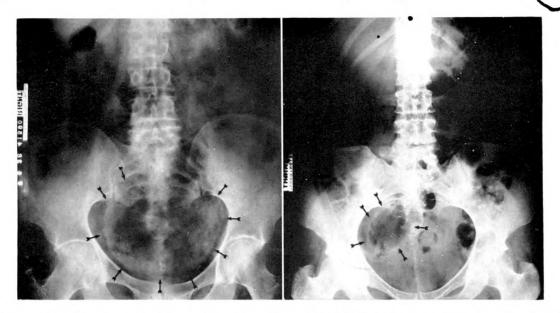


Fig. 4 (*left*). Note the marked degree of mottling. The small calcified shadow just above the mid-point of the pubis probably represents an incomplete tooth formation. The sharp demarcating ring adds to the contrast to the surrounding soft tissues.

Fig. 5 (right). The ovoid area of increased radiance is well outlined. The dense wall surrounding the area is sharply defined and is characteristic of a dermoid cyst.

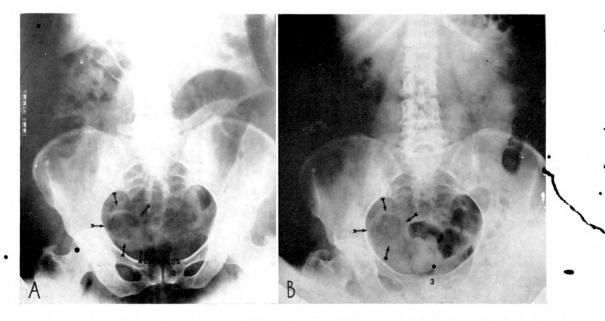


Fig. 6. A, the ureteral calculus is about the same size as the calcified bodies within the cyst. An irregular calcified plaque is present in the superior portion of the cyst wall. B, the calculus has been passed. Note the contrast to the intestinal shadows on the other side of the pelvis.

inferior portion of the cyst, probably representing a tooth formation. The whole area was confined within a contrasting ring of increased density (Fig. 4). A roentgen diagnosis of dermoid cyst was made. Operation was deferred because of the extreme age of the patient.

Case v. (Fig. 5) A. W., aged thirty-nine. This patient was referred for urologic studies, at which time a film revealed, in the vicinity of the right ovary, an ovoid area of decreased density. This area stood out in contrast to the surrounding denser tissues and this contrast was made more marked by an encircling ring of increased density. The contents of the rounded area showed a mottled appearance. Two later examinations showed the same features noted at the first examination. These constant findings warranted a diagnosis of dermoid cyst. No operation was performed.

Case VI. S. S., aged fifty-four. The history included right-sided abdominal pain, frequency and dysuria. At the first examination (Fig. 6A) a small, right ureteral calculus was noted. Just above the calculus and in the region of the right ovary was a rounded area of decreased density, banded and mottled in appearance, and encircled by a dense ring shadow. Small foci of irregular calcifications were noted within the mass. In addition, part of the wall showed a relatively denser area, suggesting a plaque of calcification. A diagnosis of right ureteral calculus and right ovarian dermoid cyst was made.

The ureteral stone was passed and a second roentgenogram (Fig. 6B), taken two months later, showed no evidence of any calculi. The rounded area in the region of the right ovary persisted, similar in size, shape and appearance to the mass noted at the previous examination. In view of the constant findings, it was felt that a diagnosis of dermoid cyst was warranted. A third film, taken a year later, showed no change in size or appearance of the cyst.

This case demonstrates the fact that repeated examinations in the presence of suspected dermoid cyst of the ovary shows constant findings which differentiate a cyst from confusing shadows due to intestinal gas.

#### DISCUSSION

Films of the pelvic abdomen in the 6 above-described cases showed masses which, except for size, resembled each other closely in appearance. The mass was always found in the pelvis and usually in the vicinity of one of the ovaries. If the cyst was large, it occupied the greater portion of the pelvis, as in Cases II and IV. The diminished density of the mass is explained

by the nature of the contents of the dermoid cyst, a sebaceous material which is liquid at body temperature. Dermoid cysts all contain varying quantities of hair mixed with the sebaceous material; this accounts for the banded, mottled appearance so characteristic of these ovarian tumors. Case IV shows the mottling especially well. All the cases show a definite capsular ring of increased density; this is explained by the capsular structure of the dermoid cyst which is made up of thickened stratified squamous epithelium and supporting fibrous tissue. An occasional plaque of calcium is noted in the wall, as in Case vi.

These characteristics, in the absence of calcification, have been sufficient to make a roentgen diagnosis of dermoid cyst and have also aided in the differential diagnosis of calcified shadows of doubtful origin in the pelvis. This is illustrated in Case vi where both a ureteral calculus and calcified parts of the dermoid cyst were present. After the passage of the calculus, the remaining calcified shadows were easily identified as cyst contents. The criteria described above should also facilitate the differential diagnosis of dermoid cysts in the presence of vesical calculi, phleboliths, calcification in the ovary, calcified fibroids, calcified glands, and healed tuberculous salpingitis with calcification.

#### SUMMARY

Criteria for the roentgen diagnosis of dermoid cysts of the ovary are presented which make the diagnosis possible in the absence of formed calcified shadows. A rounded or ovoid mass of diminished density, banded and mottled in appearance, is noted in the pelvis. The mass is encircled by a well defined ring of increased density, sharply delineating the mass from the surrounding soft tissues. These roentgen features of the dermoid cyst are also useful in differential diagnosis when a calcification in a dermoid must be differentiated from other calcified shadows in the pelvis, such as ureteral and vesical calculi, phleboliths,

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calcification in the ovary, calcified fibroids, calcified glands and healed tuberculous salpingitis with calcification.

Six cases are presented to illustrate the roentgen diagnosis of dermoid cyst of the ovary; in three of them the diagnosis was confirmed by operation.

#### REFERENCES

- ALLENDE, C. I. Roentgen diagnosis of unsuspected dermoid cyst. Bol. y trab. de la Soc. de cir de Buenos Aires, 1933, 17, 692-695; also, Rev. de cir de Buenos Aires, 1933, 12, 694-697.
- 2. Benassi, E. Roentgen diagnosis of dermoid cysts. Radiol. med. 1928, 15, 677-683.
- 3. Ewing, J. Neoplastic Diseases. Third edition. W. B. Saunders Co., Philadelphia, 1928.
- 4. Galifi, L. Diagnostic value of roentgen study in dermoid cysts. Radiol. med., 1937, 24, 888-889.
- 5. GLASS, M., and ROSENTHAL, A. H. Study of dermoid cysts with suggestion as to use of

- x-ray in diagflosis. Am. J. Obst. & Gynec., 1937, 33, 813-820.
- 6. HEFFERNAN, R. J. Dermoid cyst diagnosed by x-ray. Am. J. Obst. & Gynec., 1936, 32, 507-508.
- 7. MARION, J. Roentgen diagnosis of dermoid cyst. Lyon méd., 1929, 143, 721-723.
- 8. MARSHALL, J. M. Diagnosis of dermoid cyst of ovary. Proc. Staff Meet., Mayo Clin., 1928, 7, 4.
- OPPENHEIMER, W., and HOFER, R. Dermoid cyst of right ovary with calcified wall. Röntgenpraxis, 1932, 4, 914-915.
- 10. Rusconi, M. Roentgen diagnosis of dermoid cyst. Clin. ostet., 1934, 36, 547-554.
- II. SAUPE, E. Roentgenogram of dermoid cyst. Röntgenpraxis, 1936, 8, 109-110.
- 12. Schultze, G. K. F. Myoma and ovarian tumors in the roentgenogram. Röntgenpraxis, 1932, 4, 849-855.
- 13. SPILLMAN, R. Dermoid cysts of ovary; roentgen observations. Arch. Surg., 1929, 18, 1298-1303.





## CALCIFICATION OF THE PERICARDIUM\*

#### REPORT OF A CASE IN A BOY AGED TWELVE

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WHILE calcification of the pericardium is a common post-mortem finding, the clinical diagnosis presents many difficulties. Few cases have been diagnosed during the lifetime of the patient and these always by roentgenographic methods. A survey of the recorded instances of patients presenting definite evidence of calcification of the pericardium will show that they are mostly from higher age groups. Consequently, the following case seemed to us worthy of recording on account of the youth of the patient and the marked degree of the process.

#### REPORT OF CASE

R. F. (No. 449) was first seen on January 27, 1934, at age of nine and a half. The chief complaint at this time was cyanosis on slight exertion of a year's duration. When first noted by the mother of the patient the cyanosis appeared only when running or when entering cold water at the seashore. When patient consulted the family physician for cough at this time cardiac enlargement was first noted. A few weeks later swelling of the abdomen appeared and the patient was tapped for the first time a month before this examination. No edema of the feet. Slight dyspnea on moderate exertion.

hast Medical History. Negative for rheumatic infection of any type. Measles, whooping cough and chickenpox in infancy. Rickets diagnosed at age of eight months. At age of four patient had abscess of right ear with uneventful recovery. The tonsils were removed later the same year.

Social History. Attends school (4B). Born New York City and always lived there. Birth a version and labor long and hard. No cyanosis at birth. Walked at sixteen months. Talked at eighteen months.

Family History. Mother and father living and well. Three siblings, all living and well. The maternal grandmother had diabetes. The maternal grandfather had tuberculosis. The pa-

ternal grandfather had hypertensive cardiovascular disease. No history in family of rheumatic infection.

Physical examination at this time showed no appreciable increase in cardiac size. A blowing systolic murmur was heard transmitted to axilla. The abdomen was large and the liver was palpable a hand's breadth below the costal margin. Free fluid was demonstrated in the abdominal cavity.

An electrocardiogram was made at the time patient was first seen (Fig. 1A). The blood count: red blood cells 3,970,000, hb 69 per cent. Differential normal. Wassermann and Kahn tests normal. Blood urea 10 mg. per 100 cc. Glucose tolerance normal. Blood sugar 100 mg. per 100 cc.

The patient was advised to enter the hospital to confirm tentative diagnosis of Pick's disease but was not seen until May 4, 1936, when he was admitted to the service of Dr. E. Bacon at the Woman's College Hospital. At this time chief complaints were fluid in abdomen for three years, edema of legs for nine months and edema of face for three months.

The patient had obviously lost ground since last seen. No further growth was noted, the abdomen was tightly distended with fluid, the face and legs were edematous, cyanosis was present and a moderate degree of dyspnea was present on slight exertion. He had been tapped at least once a month since last seen but on each occasion the abdomen filled again very quickly. He stopped school ten days ago and bed rest improved his condition slightly.

Examination showed edema of the face more marked on the right side. The teeth, nose and throat were negative. The anterior cervical glands were slightly enlarged. The jugular veins were quite prominent on both sides. The anteroposterior diameter of the thorax was unusually wide. The chest was barrel shaped with flaring of the lower ribs. No left-sided precordial bulging was seen. There was no retraction of interspaces. More expansion was felt to occur in anteroposterior direction than laterally on deep inspiration. There was no tracheal deviation.

<sup>\*</sup> Read before the Philadelphia Roentgen Ray Society, November 4, 1938.

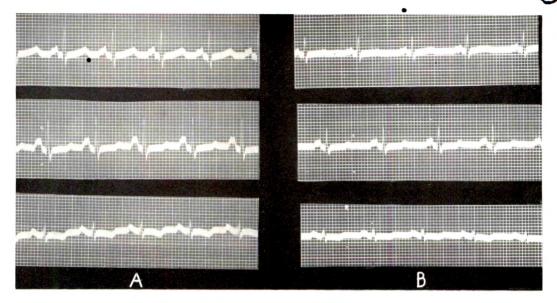


Fig. 1. A, January 27, 1934; B, May 5, 1936.

Abdomen distended. Fluid readily demonstrated. No distention of superficial veins was seen. No inguinal adenopathy. The liver was enlarged and smooth and the edge could be made out 9.5 cm. below the costal margin. Spleen not palpable. No other masses felt.

Cardiac Examination. Blood pressure: right arm, 94/62; left arm, 88/64. Apex beat palpated in the 4th intercostal space about 1 cm. to left of the mid-clavicular line. It did not move on change of position. The heart sounds were of good quality, rhythm regular, rate 86. The aortic second sound slightly louder than the pulmonic second sound. There was a systolic murmur heard over the apex and a faint mid-diastolic murmur in the same region. No thrill was palpable over any valve area.

Extremities were normally developed. All reflexes normal. Slight pretibial edema present.

A second electrocardiogram was made (Fig. 1B). A decided decrease in voltage was noted when compared to previous examination. Notching of the P-waves, particularly in lead 2, is seen together with changes in the T-waves. No axis deviation was demonstrated with change in position.

Roentgen examination of the chest (Figs. 2 and 3) showed a circle of calcium in the pericardium. Diminished amplitude of the cardiac impulse was seen on roentgenoscopy. The heart was slightly above upper limits in size. The cardiothoracic ratio measured 0.48. There was fullness in the region of the left auricle. The supracardiac shadow was wider

than usual, either due to dilated vessels, enlarged lymph nodes or effusion between the lung and mediastinum on the right—probably the latter. There was some pleural thickening over both lungs with a moderate pleural effusion of the right side.

A roentgenogram of the abdomen showed a moderately enlarged liver, the measurements from the right border to the dome of the right diaphragm being 19 cm. This was about 5 cm. above the upper limits of normal. The spleen was slightly enlarged. The kidneys were within normal limits in size, smooth in outline and occupied normal positions. There were no abnormal calcifications within the abdomen. The abdominal wall was slightly thicker than usually compatible with thickening of the paritoneum.

Roentgenograms of the long bones showed no evidence of bone or epiphyseal changes.

Impression: Findings compatible with clinical diagnosis of polyserositis. Calcification in the pericardium marked.

Examination of the urine was normal on three occasions. The blood count showed improvement since the last examination: red blood cells 4,250,000, hb 86.6 per cent (Sahli), white blood cells 7,800. Differential: neutrophiles, 72 per cent; lymplocytes, 19 per cent; monocytes, 6 per cent; cosinophiles, 3 per cent. Sedimentation time: 18 mm. in seven hours. Icteric index, 10; hemolysis, 0.40 to 0.28 per cent.

Blood Chemistry. Urea nitrogen•11 mg. per

100 cc., cholesterol 90, phosphorus, 2.44, calcium 7.9, glucose 69.5. Urea clearance normal. Ascitic fluid: total chlorides 630 mg. Albumin three plus. Culture of ascitic fluid, no growth. Mosenthal, normal range of figures.

Clinical Diagnosis. (1) Etiological, unknown; (2) anatomical, slight cardiac enlargement, mitral regurgitation, pericardial adhesions with calcification of the pericardium; (3) physiological, normal sinus rhythm; (4) functional classification, Class 2b (faulty diastolic filling).

The patient appeared to be declining very fast. The jugular veins were more distended and the abdomen filled quickly after each weekly tapping. The procedure caused the patient much discomfort and considerable apprehension. There was continued venous hypertension following abdominal tap, the readings averaging 190 mm. The situation was explained to the parents and pericardiectomy advised.

The child was moved to the Mayo Clinic and operated on the following week. The following note received from Dr. Samuel Amberg describes the findings:

The pericardium was found to be adherent to the heart throughout its entire extent and a layer of calcium was present throughout its entire attachment, the deposit being most marked along the diaphragmatic portion of the pericardium and about the inferior vena cava. On the other areas it was granular and piled up in character. The entire peri-

cardium was separated from the heart muscle, the left ventricle freed first and the calcium removed from around the pericardium and vena cava orifice. About two-thirds of the pericardium was removed entirely freeing the vena cava and heart muscle. It was a very difficult and extensive procedure because of the firm attachment of the calcium to the pericardial layers. In fact, some of the calcium had to be left attached to the auricle and inferior vena cava. Considering the magnitude of the operation the patient stood the actual procedure very well. During the night following the operation the patient showed good response. During the second day there was a gradually increasing respiratory difficulty with a steady fall in blood pressure. In spite of the usual supporting measures, oxygen and transfusions, the patient died on the morning of the third postoperative day. No autopsy was obtained.

#### DISCUSSION

Although Morgagni<sup>1</sup> is usually credited with the publication of the first case report of pericardial calcification in 1762, Dionis<sup>2</sup> gave a clear description of the condition in 1705. In 1768 Bordenave<sup>3</sup> reported a case showing calcification of the pericardium to the extent of an inch in a patient of fifty, who died of congestive cardiac failure. The first case report containing an illustration of the condition appeared in 1783 and was given by Simmons and Watson.<sup>4</sup> Here the finding of the pericardial calcification was

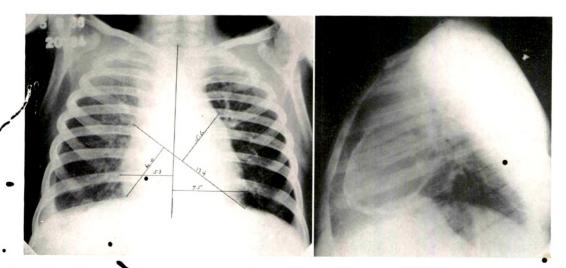


Fig. 2 (left). Posteroanterior roentgenogram of chest. There is an increase in diameter of the base of the heart but no increase in the transverse diameter. There is increase in the transverse diameter of the supracardiac shadow due to dilated superior vena cava. There are congested pulmonary vessels, with pleural thickening and effusion. Calcification not discernible with the usual exposure in this projection.

. Fig. 3 (right). Lateral projection of the chest of the same patient as in Figure 2. Note extensive calcification at periphery of cardiac silhouette. There is an increase in the anteroposterior diameter of the chest.

entirely accidental, the patient dying of carcinoma of the esophagus and no symptoms of heart disease were recorded during life. Watson suggests, "the measure of every morbid ossification will no doubt depend much on the abundance of creta in the habit. That it does abound in some and that it is very deficient in other constitutions we are fully convinced . . . " In 1809 Burns<sup>5</sup> for the first time reported a patient with a heart "... diseased with specks of bone ...," and in 1849 Rokitansky demonstrated a case of apical calcification and described the microscopic appearance of calcium granules deposited between the necrotic muscle fibers. It was not until 1910 that Schwartz reported a case of pericardial calcification recognized for the first time during the life of the patient. This was done using the roentgenologic method.

Calcification of the pericardium, if we are to judge from the number of cases reported in the literature, is a rare lesion. Turner, searching the literature in 1924, reports 89 cases and adds 3 of his own. Smith and Willius in 1932 reported 15 cases in which presence of calcification was diagnosed during life and proved at necropsy. In their series the youngest subject was twenty-four years of age and the oldest eighty-four. The average age of the series was 48.6 years.

#### ETIOLOGY

In the reported cases no general agreement exists in regard to the etiology in calcification of the pericardium. Most cases are first encountered at autopsy and the etiological factor remains obscure because evidences of the original infection cannot be determined with accuracy. The pathological identification markings are buried in the obscurity of the fibrous tissue and calcium. Few cases have been followed with accurate records from the acute stage to the stage of calcification to establish a cause and effect relationship. Youmans<sup>9</sup> and Youmans and Merrill, <sup>10</sup> in a study of 3 cases of their own and after reviewing the

histories of collected cases, favor tuberculosis as the commonest etiologic agent in. · most instances. However, Bellet and Mc-Millan, 11 in a study of 100 cases of tuberculosis of the pericardium at the Philadelphia General Hospital, did not find calcification in a single instance. Smith and Willius<sup>7</sup> did not find any evidence of tuberculosis in their series of cases. The single etiological factor that affected the largest number of cases in their group was rheumatism. A few cases undoubtedly are of this origin. It is likewise true that many previously undiagnosed inflammations about the pericardium at the time of an influenzal or pneumococcic infection are the starting points of the process that later receives the deposits of calcium. Rarely is syphilis the cause. Of all the etiological agents mentioned above, the pneumococcus is the most likely one to leave behind the proper soil for the development of calcification. The pericardium lies in contact with the mediastinal structures and an inflammatory process arising in the course of an influenzal, pneumococcic, rheumatic or streptococcic infection can easily spread with initial involvement of all these important structures. The etiological agent in scarlet fever is closely allied to the organism responsible for the rheumatic state and it is not unlikely that inflammatory changes occur in the course of scarlet fever and result in the production of necrotic tissue soil for the deposit of calcium.

A number of factors have been claimed to influence the deposit of calcium saits in the pericardial tissues. The best soil is prepared by a mass of necrotic tissue in this locality that receives a poor blood supply. A local increase in the alkalinity of the blood at times renders the calcium salts less soluble and more likely to deposit. This will occur more often in individuals who have an overloading of the blood with calcium and phosphate salts. Factors that act from time to time to cause concentration of the blood under these favorable conditions may assume the role of immediate causes. The vitamins and the hormone.

of the parathyroid glands have likewise been mentioned as agents in the process.

Sex is a factor. In all the series reported in the literature males are more often affected than females in the ratio of 3:1.

Regardless of the etiological factor, the inflammatory process involving pericardium and mediastinal structures may burn itself out with the formation of some fibrous adhesions between the lavers of the pericardium, in which event little harm results. If, however, as in this case, calcium appears early and is deposited all over the pericardial surface, symptoms of a cardiac nature are soon seen. The amount, degree and location of the calcium and its association with adherent pericarditis are the important points. The heart in this patient produced symptoms when it sought to attain its normal growth in a restricted space. If there is a valvular lesion in addition, the embarrassment will occur sooner. Firm attachment of the heart to surrounding structures by extrapericardial adhesions may complicate the picture still further by limiting cardiac contraction. Operation on this patient showed that the calcium deposits about the orifices of the superior and inferior vena cavae were the main factors in influencing the clinical course. The encroachment on the lumen of these vessels gives rise to certain recognizable syndromes. With involvement of the superior vena cava the obstruction to the return flow of blood from the face and neck causes edema in these regions. Evidence of the increased venous pressure in this part of the body is seen in the engorgement of the veins of the neck and cyanosis. The venous pressure readings is this boy were always markedly elevated. If the flow is obstructed in the pulmonary artery, pulmonary hypertension and right ventricular strain result. In obstruction of the inferior vena cava we note enlargement of the liver to a much greater size than is usually found in cases of congestive cardiac failure, ascites, edema of the legs and hydrothorax. These are out of proportion to signs of involvement in

the lesser circulation. Low blood pressure is a common finding and nearly always a low pulse pressure.

#### CLINICAL DIAGNOSIS

In most cases the presence of the signs above described lead to an initial diagnosis of progressive cardiac failure. However, suspicion should be aroused when the heart size is much below the expected picture. The finding of cyanosis is another important point in the diagnosis that should lead to a thorough roentgen study. An early, correct diagnosis of calcification of the pericardium is extremely important, for if the signs presented are attributed to other factors it will prevent the consideration of operative relief now proved to be of outstanding value in the treatment of these cases. The formation of the chest in this case was significant for we do not find a barrel-shaped thorax in one so young without good reason. In this patient there was more expansion in the anteroposterior plane than laterally. The apex beat was fixed but no retraction of the ribs and interspaces was noted. Today, when roentgenoscopy in these cases is usually first carried out by the internist, the discovery of the "small, quiet heart" may give the first clue and the presence of calcification demonstrated on subsequent plates may determine the diagnosis.

The electrocardiogram in the patient reported here is interesting (Fig. 1). Comparing the one taken on January 27, 1934, with the one obtained on last admission a striking change will be seen. The first tracing is normal with the exception of P-wave notching and a slight depression of the S-T intervals in lead 2. In the last tracing the difference in the amplitude or voltage of the QRS groups and the flat T-waves should be noted. This change is not an infrequent finding in cases of calcification of the pericardium particularly after the development of extensive anasarca.

Reviewing the auscultatory findings in the case reported here we note that a murmur was heard over the region of the apex

in mid-diastole. There was considerable discussion at the time over the interpretation of this extra sound thought by some to be a murmur significant of a stenotic lesion of the mitral valve and by others to be an unexplained extra sound in the middle of diastole. Considering the marked alterations in the tissue structure and the increased density of the calcified pericardium an extra sound in diastole would seem to be a reasonable finding. However, it was not until reading the recent article by Lian, Marchal and Pautrat<sup>12</sup> that the significance of the sound we heard over the apex in diastole in this patient became clearly understood. These authors describe a sound protodiastolic in time in 2 cases of calcification of the pericardium that is louder at times than the heart sound giving a gallop rhythm best heard between region of the apex and end of sternum. This extra sound (described as a vibrance) should always lead the clinician to make a thorough study for the presence of calcification. It has a peculiar vibration that other sounds, occurring at this time in the cardiac cycle, do not have and this quality serves to distinguish it. The physiological reduplication of the second heart sound is best heard over the base. The physiological third heart sound does not have the intensity nor the vibration that this extra sound possesses. The mid-diastolic mitral stenotic murmur is not accentuated nor as loud as this vibrance but, as in this case, mitral stenosis is often suspected because it is the commoner lesion. Roentgen examination serves to make the differentiation. In the case of mitral stenosis, there is mitralization of the left cardiac border and if the sound arises from this type of pericardial involvement, we see the calcium. Bouillaud may have heard this sound for he speaks of a case of a myocardial stony projection into the pericardium giving a scraping sound but he does not describe it further nor does he mention the time in the cardiac cycle.

However, in many cases the different signs and symptoms that we have described may prove inconclusive. The main diagnosis then rests upon the roentgen findings.

## ROENTGENOLOGICAL ASPECTS

A good roentgenologist must first be a good clinician. In the presence of any or all of the above manifestations, chronic adhesive pericarditis with calcified pericardium should be suspected and the following roentgenologic evidence sought:

- 1. Absence of cardiac pulsations or diminished amplitude of pulsation.
- 2. Slight cardiac enlargement with disproportion between the degree of circulatory embarrassment and the size of the heart.
- 3. Irregularity and haziness of the cardiac silhouette due to external adhesions uniting the pericardium to the pleura, adjacent mediastinal tissues, thoracic wall or the diaphragm.
- 4. Inability of the heart to change its position during the various phases of respiration.
- 5. Increase in the transverse diameter of the supracardiac shadow, due to stasis in the venous circulation, with dilatation of the veins.
- 6. Presence of calcification in the pericardium.
  - 7. Characteristic kymographic changes.
- 8. Fixation of the dome of the left diaphragm.
- 9. Elevation of the diaphragm and limitation of the respiratory excursion with small pleural effusion.
- 10. Increase in the lung markings due to congested pulmonary vessels with stasis in the lesser as well as the greater circulation.

The cardiac measurements in our case were 5.3 cm. from midline to right border, 7.5 cm. from midline to left border; the cardiothoracic ratio was 0.48, the length of the heart was 13.4 cm., and the diameter at the base was 11.6 cm. These two measurements, particularly the diameter at the base, are definitely above the upper limits of normal.

The case reported by us in this communication showed the above changes. It should be noted that the calcification can only be seen in the oblique projection and, not in the anteroposterior projection.

It is important to make a differential diagnosis from the film between calcified pericardium and calcification of the heart muscle or endocardium. Calcification of the heart muscle is usually seen in older individuals. This type of calcification is not at the periphery, it involves smaller areas and is not associated with such absence or such marked diminution of the cardiac impulse as occurs in calcification of the pericardium.

#### TREATMENT

The only treatment is surgical. Success follows early diagnosis, good preparation of the patient and the selection of an experienced surgeon. The procedure is the removal of the mechanical impediment to the circulation and there are several types of operation.

Brauer<sup>13</sup> in 1902 first suggested subperiosteal resection of the left fourth, fifth and sixth ribs with their cartilages, extending from the mid-clavicular line or beyond to the sternum. This procedure allows greater freedom of movement for the heart and does not involve a great risk. Properly carried out it is attended with little shock and the relief obtained warrants more common employment in these cases.

Another type of operative procedure called for in the case reported here is the removal of portions of the pericardium from, the heart itself, particularly the ventricle. At the same time the layer of calcium is removed from around the orifice of the inferior vena cava. Results achieved by this type of surgery are the most brilliant in medicine. A number of striking cases of relief and cure have been reported by White,14 Churchill,15 Beck and Griswold,16 and Flick and Gibbon.17 Improving surgical techniques and closer cooperation between internist, roentgenologist and surgeon in the handling of these patients point to an even more promising future for this field.

#### SUMMARY

1. A case is presented in detail of a boy, aged twelve, who showed a combination of

calcification and adherent pericardium resulting in Pick's syndrome with pleural effusion, ascites, large liver and edema of the extremities. In this patient operative relief was attempted.

2. A discussion of the incidence, etiology, clinical and roentgen diagnosis of calcification of the pericardium is given. Early diagnosis and the benefit of surgical treatment are emphasized.

#### REFERENCES

- 1. De sedibus et causis morborum. Epist. 27, Art. 16.
- 2. L'anatomie de l'homme, suivant la circulation du sang, (etc.) Pierre Dionis. Fourth edition. L. d'Haury, Paris, 1705, p. 699.
- 3. Bordenave, M. Mém. Acad. de sc., Paris, 1768.
- 4. Simmons and Watson. London Med. Communications, 1783, p. 228.
- 5. Burns. Diseases of the Heart. Edinburgh, p.
- TURNER, H. H. Calcification of pericardium; review of the literature. *Internat. Clin.*, 1924, 4, 137–155.
- 7. Smith, H. L., and Willius, F. A. Pericarditis. *Arch. Int. Med.*, 1932, 50, 171-202; 410-418.
- 8. WILLIUS, F. A. Clinic on chronic adherent pericarditis with calcification of pericardium. *Proc. Staff Meet.*, Mayo Clin., 1936, 11, 312–317.
- YOUMANS, J. B. Calcification of pericardium; two cases diagnosed during life. Ann. Clin. Med., 1926, 4, 1032–1044.
- YOUMANS, J. B., and MERRILL, E. F. Calcification of pericardium; report of a case. J. Am. M. Ass., 1924, 82, 1833–1838.
- 11. Personal communication.
- LIAN, C., MARCHAL, M., and PAUTRAT. Clinical sign of calcification of the pericardium. Bull. et. mém. Soc. méd. d. hôp. de Paris, 1933, 49, 20–28.
- 13. Brauer, L. München. med. Wchnschr., 1902, 49, 1072. Also: Die Kardiolysis und ihre Indicationen. Arch. f. klin. Chir., 1903–1904, 71, 258–267.
- 14. White, P. D. Heart Disease. Macmillan Co., New York, 1931.
- 15. Churchill, E. D. Decortication of the heart (Delorme) for adhesive pericarditis. *Arch.* Surg., 1929, 19, 1457–1469.
- 16. Beck, C. S., and Griswold, R. A. Pericardiectomy in treatment of Pick syndrome. *Arch. Surg.*, 1930, 21, 1064-1113.
- 17. FLICK, J. B., and GIBBON, J. H., JR. Pericardiectomy for advanced Pick's disease. *Arch. Surg.*, 1934, 29, 126–137.

## SILICOSIS AND TUBERCULOSIS ROENTGENOLOGI-CALLY SIMULATING A NEOPLASM

## REPORT OF A CASE

By ERNST A. POHLE, M.D., Ph.D., Professor of Radiology, and GORTON RITCHIE, M.D., Associate Professor of Pathology University of Wisconsin Medical School

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SILICOSIS usually produces a fairly typical picture in the roentgenogram, the lesions being seen in the periphery of the lungs. The differential diagnosis can be made as a rule on the basis of exposure of the individual to dust. The case here reported is quite exceptional in that the roentgen findings were very suggestive of a neoplasm while the autopsy revealed only hilar silicosis and tuberculosis. Furthermore, it was impossible to find a source of silica.

#### CASE REPORT

A white male, aged thirty-six, was admitted to the State of Wisconsin General Hospital on November 26, 1937, with the complaint of shortness of breath, which was especially marked upon any physical activity. Before coming to Wisconsin he had had a radical antrum operation in Texas without relief of his symptoms. The pertinent findings upon physi-

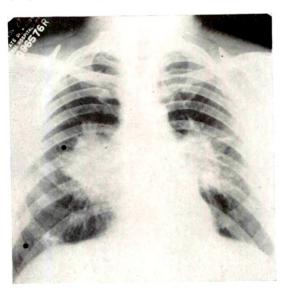


Fig. 1. Roentgenogram taken November 27, 1937, in Madison.

cal examination were some weight loss, a few pulmonary râles and a prolongation of the inspiratory and expiratory note upon auscultation. In addition he had a tachycardia.

Roentgenograms of the chest showed a large irregular mass projecting from the right mediastinum into the lower lungs, and a similar smaller mass with fuzzy edges was seen projecting on the left side (Fig. 1). There was a little shrinkage of the left upper lobe with thickening of its interlobar pleura. The lungs were elsewhere clear. The bizarre findings in the chest were very strongly suggestive of a primary bronchogenic carcinoma with bilateral lymphatic spread. Roentgen examination of the sinuses showed an opaque maxillary antrum, the remaining sinuses being clear.

Bronchoscopic examination was done; it revealed some stenosis below the bifurcation of the major bronchi on the right side, apparently due to some pressure from without rather than from a growth within the bronchial tree. Since surgical removal seemed to be impossible it was decided to give roentgen therapy a trial. From December 2 until December 17, 1937, he received, as an outpatient, a total of fourteen exposures over the anterior and posterior mediastinum, 200 r (in air) per field, halfevalue layer of copper 1.35 mm. The skin erythema had developed by the time of the last treatment, and the patient was asked to return for re-examination within three weeks. However, he insisted on returning to Texas and in order to permit a proper follow-up, he was referred to a radiologist near his home town for examination and treatment if indicated.

On January 26, 1938, he was admitted to the local hospital in Texas with a temperature of 102.6° F. and a pulse rate of 112. Roentgen examination showed no appreciable change of the process in either hilar region but there was considerable infiltration at the right base, and the left upper lobe looked more cloudy (Fig. 2). Four additional treatments were then

given through left and right oblique fields in · order to avoid the previous portals of entry which still showed marked pigmentation. The patient began spitting up some purulent material and seemed to be steadily declining. He desired then to return to Madison and was placed on the train. He died en route and a partial post-mortem examination was made in Oklahoma. At that time most of the right lung and heart were removed and placed in a glass container to be sent here for further study. The examiner in Oklahoma did not find sufficient pathology to cause death. Our own postmortem findings follow:

Autopsy Report. The body had been embalmed, and a partial autopsy had already

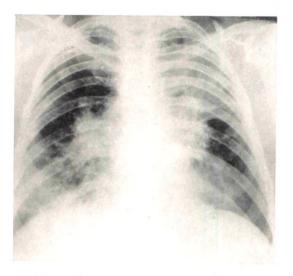


Fig. 2. Roentgenogram taken on January 29, 1938, in Texas.

been performed as described above. Lungs: The two lungs were essentially similar, and so will be described together. The pleura was smooth and glistening, and no adhesions or fibrous tags could be found. The hilar portion was very dense and fibrous; this fibrous area involved about one-third of the volume of each lung, and was irregular in shape. The bronchi running through the dense area were thickwalled and had evidently been compressed by the contraction of the surrounding fibrous \*tissue. The peripheral portions of the lungs were air-containing, although the framework was somewhat thickened. Carbon pigment was present throughout, but was especially dense in the hilar forous portion.

Microscop cally, the lesion at the hilum was

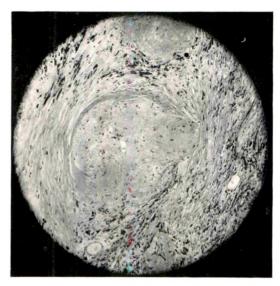


Fig. 3. Silicotic nodule.

composed of very dense fibrous tissue nodules, chiefly perivascular in distribution, but coalescing to form a dense mass (Fig. 3). A few tubercles containing giant cells were seen (Fig. 4), and several areas of caseation were present. One calcified area contained bone with a small area of bone marrow. The peripheral portions of the lungs were the site of unresolved and organizing pneumonia. Many large epithelial cells were noted in the alveoli, but these were diffusely distributed and did not suggest tumor

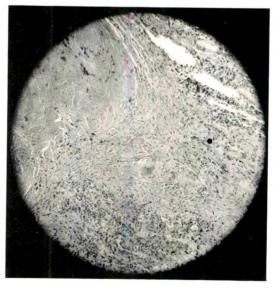


Fig. 4. Showing tubercle with giant cells in central portion and heavy fibrous tissue reaction.

growth. A few of the vessels contained organized and canalized thrombi.

Examination of the remaining organs revealed no lesions relevant to this report, except that a few early miliary tubercles were seen in the spleen.

Pathological Diagnosis: Silicosis and tuberculosis at the pulmonary hilum; pneumonia with delayed resolution and partial organization.

Chemical examination of the lung tissue by Dr. Frank L. Kozelka of the Department of Pharmacology and Toxicology gave the following results:

	Grams—		
	dry wt.	$\mathbf{A}\mathbf{s}\mathbf{h}$	SiO <sub>2</sub>
Sample 1	3.0355	2.18%	0.92%
Sample 11	5.8873	2.23%	0.92%

Expressed differently, each sample contained 9.2 mg. of SiO<sub>1</sub> per gram of dried tissue, which is far above the 1.13 mg. determined by McNally<sup>1</sup> as the average content for normal lung.

#### COMMENT

In reviewing this case, even in the light of the post-mortem findings, we still believe that a roentgenological diagnosis of neoplasm was justifiable. The only question arising at the time of the radiological consultation was as to the specific nature of the process. Because it was bilateral one might have hesitated to look upon it as a primary bronchial malignancy, since the supposed metastatic extension occurred in a manner which is quite unusual with this disease. One might have been more inclined to consider it a metastatic glandular lesion or a malignant lymphoma. While part of the radiopacity was perhaps due to atelectasis, it does not seem justified to explain it entirely on that basis, since the involvement followed neither lobe.

We are dealing with an extremely unusual distribution for silicosis, which is typically seen in the peripheral portions of the lung. The extreme dyspnea in this case was undoubtedly caused by the contraction of the hilar scar tissue about the main bronchial trunks.

#### SUMMARY

A case of silicosis and tuberculosis in a white male, aged thirty-six, is reported, which roentgenologically had the appearance of a neoplasm. There was no history of exposure to dust containing silica. The post-mortem findings and the results of the chemical examination of the lungs are given.\*

\*Since submitting this paper for publication the following pertinent articles have been published: Bradshaw, H. H., and Chodoff, R. J. Anthracosilicosis simulating pulmonary carcinoma. Am. Rev. Tuberc., 1939, 39, 817–824. Holman, E., and Pierson, P. Carcinoma of the lung simulating inflammatory disease. J. Am. M. Ass., 1939, 113, 108–111.



<sup>&</sup>lt;sup>1</sup> McNally, W. D. Silicon dioxide content of lungs in health and disease. J. Am. M. Ass., 1933, 101, 584-587. The normal lung contains 1.13 mg. SiO<sub>1</sub> per gram of dried tissue (0.113 per cent).

### FLUOROGRAPHY

## THE PHOTOGRAPHY OF THE FLUORESCENT IMAGE

By I. SETH HIRSCH, M.D. NEW YORK CITY

In HIS first paper on the discovery of the x-rays, Roentgen demonstrated both the fluorescent and photographic effects of the rays. In the period of enthusiastic experimentation which immediately followed the announcement of the discovery much ingenuity was shown in the efforts to establish the best technical method of recording the roentgen image.

The screen image, simple and easy in its attainment, instantaneous in its appearance, graphic in its visibility, seemed for the moment to be the most desirable and it was only logical to attempt to obtain a permanent record of this image by ordinary photography. Thus, already in April, 1896, six months after the discovery, Blever constructed and used an apparatus for photographing the fluorescent image, which he called the photofluoroscope. Bleyer thought the method had an advantage over the direct film method in that visual observation could be combined with the production of a permanent record then obtainable by photographic exposures of a few minutes. Among other early efforts in this direction may be mentioned that of McIntyre who, by the use of a lead shield around the lens aperture, remedied the fogging of the plates in the camera arising from the direct radiation passing through the screen.

But when Porcher (1897) after considerable experimentation discarded the method as impractical and as having no advantage whatever over direct roentgenography, he apparently expressed the opinion of most workers, for the method was abandoned in favor of the direct roentgenography which developed with remarkable strides from its crude beginnings to its present state.

However, the allure of the moving picture stimulated workers to investigate the possibility of an indirect method of its accomplishment and in 1907 Köhler, who

was engaged in direct roentgen cinematography, mentioned photography of the fluorescent image as a promising future possibility, and in 1909, in association with Biesalski, described a practical method of fluororoentgenography utilizing a screen of calcium tungstate (blue fluorescence), a camera with an F 2.0 lens and a mirror which permitted placing the camera outside of the beam of direct radiation. Biesalski also used a concave mirror instead of a lens by means of which he could obtain a much greater effective optical aperture.

It was apparent that the future development of the method depended on the possibility of obtaining lenses of greater aperture, screens of brilliant luminescence and photographic films of high sensitivity.

In a paper entitled, "Photography of the Fluorescent Screen for Roentgen Kinematography and other Purposes," read before the Philadelphia Roentgen Society on March 24, 1911, Caldwell presented all the basic and essential principles underlying the application of fluorography and foreshadowed its present-day application with prophetic instinct and scientific acumen. He used a  $4 \times 5$  camera with a Cooke lens, working at aperture F 4.5 and a "Gehler folie" screen which had phosphorescent (after glow) as well as high actinic fluorescence. To determine whether the "after glow" would interfere with making successful photographs of the screen in rapid • succession, he attached the screen to a rotating disc and exposed it to roentgen rays through a narrow radial slit in a sheet of lead. A brilliant narrow line of fluorescence was produced on the screen. It was necessary to rotate the screen at an exceedingly high rate of speed in order to materially widen the brilliantly fluorescing portion, indicating that "after glow" was of no practical importance as a contaminating

factor.\* The photographs he obtained of the extremities, lungs and thorax were full of rich detail and, as he had hoped, the camera recorded much more than the eye could see on the fluorescent screen.

Caldwell pointed out the advantages of the method, the low cost, the simplification of the problems of filing and transportation. He prophesied that with the development of screens of higher actinic who in a patent suggested the use of a screen bent into a surface concave toward the lens so as to correct for some of the optical errors of the wide aperture lenses. The great improvement in recent years in fluorescent screens by Leonard Levy of London and in photographic materials, is responsible for the development of the method to such a state that its practical and routine application is now possible.

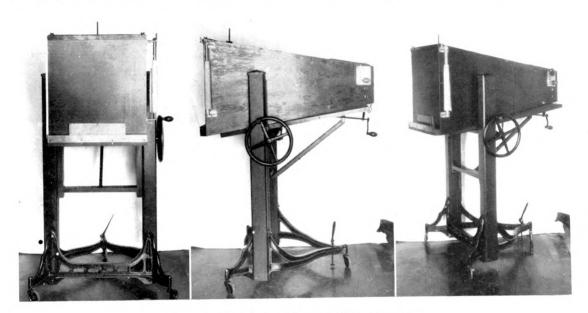


Fig. 1. Three views of fluorographic apparatus.

properties, photographic films of greater sensitivity, lenses of greater speed and more intense excitation by roentgen rays, the method would attain a great practical value and would revolutionize roentgenography.†

In 1913 Loman and Camandon used an F 1.55 lens with a specially sensitized film. Luboshez made use of an F .625 lens and still more recently Dariaux and Djian, a lens of aperture F .53. Others who should be mentioned in connection with this work are Reynolds, Reiser, and Schinzel,

\*This experiment, made twenty-eight years ago, has a bearing on modern fluorography as the most sensitive fluorescent screen now available, the "fluorazure" screen also shows an "after glow," but not sufficient to interfere with the recording of a clear image.

† I have gone into detail regarcing Caldwell's work because of the various claims which have been made for priority in this field.

De Abreu's work (Brazil) in 1930 represents the first large scale application of the method. In fact modern fluorography owes its present status to his ingenuity and enthusiasm. Many technical improvements have been devised by Janker (1938).

My own interest in this work is due entirely to the inspiration of de Abreu, whose graphic demonstration of the application of this method convinced me of the practical applicability to diagnostic roentgenology.

## APPARATUS AND TECHNIQUE

The apparatus consists essentially of a light-proof box of pyramidal shape with a fluoroscopic screen mounted on one end, a camera at the other, and means for ad-

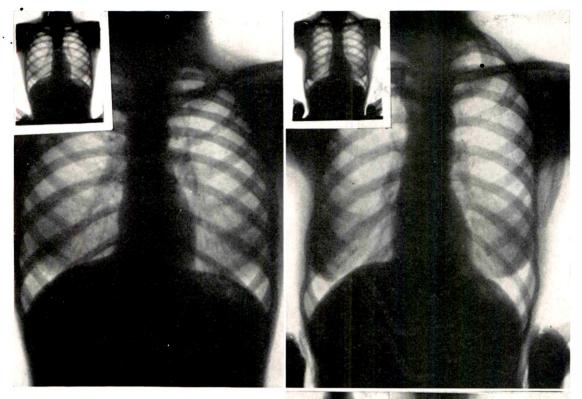
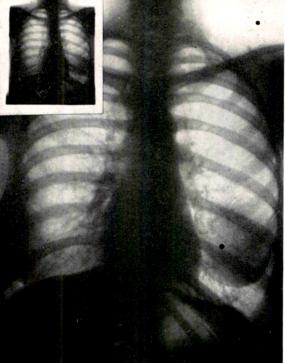


Fig. 2. Fluorograms actual size and enlargements.

justing the height of the apparatus (Fig. 1).

The screen may be of the zinc sulphide (fluorazure Patterson) type, which has a very high actinic effect, or a Patterson "B" screen. In this work, both have been used. The fluorazure screen has a definite "after glow" but, as noted above, this is not of practical importance. A 35 mm. film camera, equipped with an F 1.5 lens may be used. A slower Tens is not suited for this work and there is no faster lens ordinarily available which will cover this field. The film may be a high speed Panchromatic for use with the "B" screen, or a special film similar in its characteristics to the ordinary roentgen film developed by the Eastman Kodak Company for use with the "fluorazure" screen. The roentgenray exposure required with this material is about to live times that necessary for the same subject with the standard double-



coated roentgen film and high-speed intensifying screens. For the average chest,

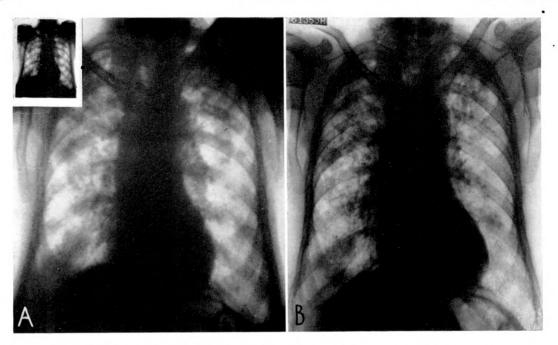


Fig. 3. Exudative and fibroid phthisis of both lungs. A, fluorogram and enlargement;
B, reduction of regular teleroentgenogram.

80 kv. (peak), 150 ma. and 1/10 second exposure at 30 inch tube-screen distance is necessary.

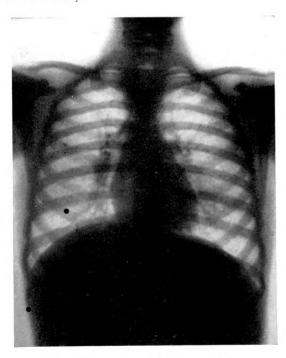


Fig. 4. Ghon focus, right lung—enlargement from fluorogram.

The camera is mounted at a distance of 90 cm. from the screen, the focus of the lens being determined once and for all by trial exposures. The camera is removable for the loading and unloading of 150 cm. of 35 mm. film, enough for thirty-six exposures. Mechanical means are provided for the winding of the film and operation of the shutter from the outside of the box. The number of exposures made is recorded on an automatic counter.

A positive method of film identification is necessary because the ordinary lead numbers are not always legible. To avoid this difficulty, the numbers and letters are recorded optically by a method similar to that used by Janker. Two light-proof slots are arranged below the screen for the insertion of white cards bearing identifying information written in black ink. Small lights inside the box illuminate these cards in such a manner that no stray light reaches the screen. These lights are controlled by a switch on the outside of the box, where a pilot light in series with the marking lights indicates that this recording feature operates properly

The processing of the strips requires scrupulous attention to small details. Insignificant dirt particles and scratches may ruin an otherwise good film. All solutions should be filtered, and the film should be processed in a suitable tank, different types of which are on the market.

#### VIEWING OF THE FLUOROGRAMS

After development, the strip bears eight fluorograms per foot of film. These may

jector and a grainless screen are necessary for optimum results. The screen and projector are conveniently mounted on a single board which may be used as a unit. The film may of course also be projected to the usual full size lecture hall screen.

#### FILING AND STORAGE

The entire roll of films may be filed in holes in a board, as is done by de Abreu, or, if cut into short strips, mounted in book

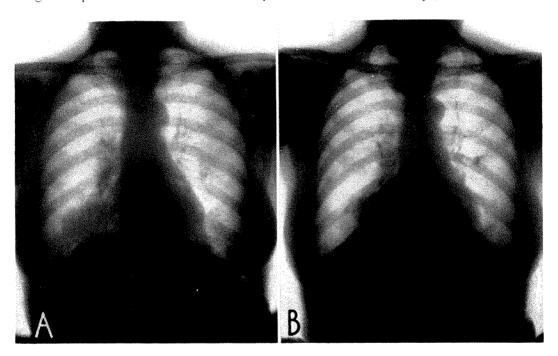


Fig. 5. A, tumor right lower lobe; tracheobronchial nodes; B, after pneumothorax—enlargements from fluorograms.

be viewed: (1) By a magnifying lens. An arrangement may be made by which the film is drawn over an illuminated surface, above which is mounted a magnifying glass. (2) By projection. By projecting the film to a magnification of 6.8 times, an image is obtained which is 15 per cent smaller than half-size of the original screen image. For the average chest, this just compensates for the distortion due to the use of 30 inch target-screen distance. Thus the projected image, under these conditions, is a true half-size representation of the chest in the average case. A good pro-

form behind celluloid, as by Janker. But for hospital work, where the films must be repeatedly consulted, it appears preferable to mount each film individually in 2"×2" slides, with a paper mask on which is written any information desired. Such a mount avoids the inevitable scratching which occurs if the film strips are handled frequently. These slides are filed in shallow filing cases.

#### EVALUATION

This fluorographic method is just now not intended as a substitute for the usual

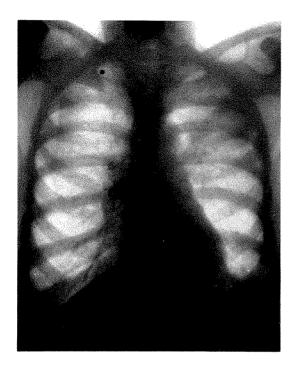


Fig. 6. Fibroid apical tuberculosis, left upper lobe extension—enlargement from fluorogram.

roentgenogram, though it seems to be developing in this direction. Generally speaking, it may be said that the record is superior to the fluoroscopic examination, not only because of the better visibility of detail, but also because it has the obvious advantage of furnishing a permanent record of the fluoroscopic image. It is well known that changes in the lung can be visualized fluoroscopically only if they have a certain size, and tests have shown that changes of small areas can be visualized on the fluorographic record which cannot be seen fluoroscopically. It is of course conceded that the small fluoro-• graphic film in no way compares with the regular film in the sharpness of the detail and contrast. But for a general gross survey of the chest, with the view of determining whether or not pathological conditions exist, the small fluorographic film may well serve as a substitute for fluoroscopy and for the regular film. For the study of the characteristics of the lesion, however, the large film is obviously the best record.

The paramount advantage of fluor-

ography is the reduction in the cost of the examination, particularly in thoracic and gastrointestinal work. The usual film of the chest (14"×17"—238 square inches) costs about 50 cents, while the film used in fluorography measures 2 square inches and costs but 2 per cent of the large film. This low cost makes possible the examination of large groups and permits roentgen-ray surveys of whole populations—an application of tremendous social value. It makes possible the routine examination of the chest and gastrointestinal tracts, for instance, of all admissions to the hospitals, and will undoubtedly aid in the early di-

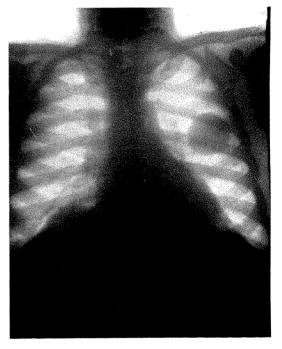


Fig. 7. Metastatic tumor left lung—enlargement from fluorogram.

agnosis of many diseases of the lungs, heart, mediastinum and gastrointestinal tract.

#### APPLICABILITY

1. Fluorography is applicable to the study of the skeleton, delineating gross bone changes and deformities.\*

\* For some years I have been making large films,  $20 \times 36$  inches, for the study of the relationship of habitus to visceral merphology, but the high cost of the roentgenograms has impeded this

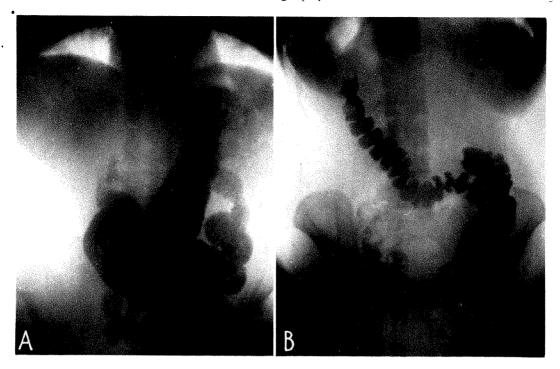


Fig. 8. A, normal stomach and small intestine; B, normal colon—enlargements from fluorograms,

- 2. It is useful in gastrointestinal surveys, particularly in the study of the colon, and in motility tests.
- 3. It gives clearly the position and shape of the heart and, if suitable correction factors are used, the heart shadow diameters may be determined according to the usual method.
- 4. Its greatest field of usefulness is in the study of the lungs, particularly for the determination of tuberculous changes. It is not intended as a method of fine differentiation as to the type of lesion, but the early apical infiltration, the cavity, the fibrotic and calcific changes are demonstrable. The image of the pulmonic fields has neither the contrast nor the detail of the large film but, nevertheless, the record is sufficiently clear to permit the differentiation of the normal from the abnormal lung.

I desire to acknowledge the invaluable assistance rendered by Myron Schwarzschild in the construction and testing of the apparatus.

work By fluorography, however, it now becomes possible to make such examinations of large groups at a very low cost.

#### REFERENCES

- 1. DE ABREU, M. Verfahren und Apparatur zur kollektiven Röntgenphotographie (indirekte Röntgenaufnahme). Ztschr. f. Tuberk., 1938, 80, 70-91.
- DE ABREU, M. Zwei Jahre kollektive Röntgenphotographie. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1938, 58, 574-587.
- 3. DE ABREU, M. A situação atual da roentgenfotografia na profilaxia da tuberculose. Rev. brasil. de tuberc., 1938, 8, 43-62.
- DE ABREU, M. Roentgen-fotografía. Rev. Asoc. méd. argent., 1938, 52, 460-463.
- 5. DE ABREU, M. Roentgen-fotografía. Arch. argent. de enferm. d. ap. respir. y tuberc., 1938, 6, 191-202.
- BIESALSKI and KOHLER. Die ersten Versuche mit indirekter Methode. Internal. Phot., Dresden, 1909.
- BLEYER. On the Bleyer photo-fluoroscope. *Electric. Eng.*, 1896, 22, 10.
- 8. Blome, K. Die Aufgaben der Röntgenologie im Rahmen der Gesamtarbeit an der Volksgesundheit. Deutsche Arzt., 1938, No. 28, 491. Also: Fortschr. a. d. Geb. d. Röntgenstahlen (Tagungshft.), 1938, 58, 15-21.
- CALDWELL, E. W. Photography of the fluorescent screen for roentgen kinematography and other purposes. Am. QUART. ROENTGENOL., 1911, 3, 34-40.

- 10. DARIAUX and DJIAN, G. Solution pratique de radioscopie cinématographie par le procédé du docteur Georges Djian. Bull. et mém. Soc. de radiol. méd. de France, 1935, 23, 344-346.
- 11. Holfelder. Mitt. a. d. deutsch. Röntg.-Kong.,
- 12. HOLFELDER, H. Verfahren und Apparatur zur kollektiven Röntgenphotographie (indirekte Röntgenaufnahme). Fortschr. a. d. Geb. d. Röntgenstrahlen, 1938, 58, 181–187.
- Janker, R. Roentgen cinematography. Am. J. Roentgenol. & Rad. Therapy, 1936, 36, 384-390.
- 14. Janker. Ergebnisse der medizinischen Röntgenphotographie. Vortrag vor der deutschen Ges. f. photogr. Forschung, Berlin, 19, VI, 1937.
- 15. Janker. Die Röntgenkinematographie. Heft 15 der Schriftenreihe der Reichsstelle für den Unterrichtsfilm. Kohlhammer, Stuttgart, 1938.
- 16. Knothe. Die Röntgenschirmbildphotographie. Deutsche Arztebl., 1938, No. 36, 593.
- Köhler. Kinematographische Röntgenvorführungen normaler und pathologischer Atmung. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1907,
   11, 292.

- 18. Lomon and Camandon. Radiocinématographie par la photographie des écrans intensificateurs. *Presse méd.*, 1911, 19, 359.
- 19. Luboshez, B. E. Cineradiografia. Radiol. med., 1931, 18, 450-457.
- 20. LÜDIN, M. Röntgenologische Thorax-Reihenuntersuchungen (Durchleuchtunge und Aufnahme) bei Studenten. Schweiz. med. Wchnschr., 1935, 65, 797-799.
- 21. McIntyre. X-rays. Lancet, 1896, 2, 1303.
- 22. Porcher. Photographie de l'image fluoroscopique. Compt. rend. Acad. d. sc., 1897, 409.
- Reiser, E. Verfahren zur Herstellung von Photographien röntgenologischer Beobachtungen. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1926, 34, 80-83.
- 24. Reynolds, R. J. Cineradiography. *Brit. J. Radiol.*, 1927, 23, 33-44; 1934, 7, 415-424. Also, Am. J. Roentgenol. & Rad. Therapy, 1935, 33, 522-528.
- Schinzel. Verfahren zur Herstellung von Röntgenstrahlenbildern. Patent. No. 544241, Klasse 57a, Gruppe 7.
- Thompson, E. P. Roentgen Rays and Phenomena of the Anode and Cathode. D. Van Nostrand Cc., New York, 1896.



## OSTEOFIBROMA OF THE CRANIUM

#### FROM A ROENTGENOLOGIC VIEWPOINT\*

· By CHARLES WADSWORTH SCHWARTZ, M.D.

NEW YORK CITY

In 1891, von Recklinghausen described the disease called osteitis fibrosa, and since then there have been many publications dealing with this interesting condition. Almost all articles and references dealing with osteitis fibrosa, or osteitis fibrosa cystica, discuss the bone changes in the skeleton below the neck, with but few exceptions which usually refer to the changes produced in the jaws. It is extremely rare to find references in the literature dealing with lesions involving the skull bones, and for that reason this discussion is offered.

The etiology of osteitis fibrosa is not well understood. When the condition is widespread and affects many bones of the skeleton, most of the evidence points to its being the result of an increase in parathyroid activity. When we find localized areas of osteitis fibrosa, such as solitary bone cysts or particularly lesions of the skull, it seems highly improbable that the parathyroids are at fault. The lesions, as we see them in the bones of the vault, are not predominantly cystic. In fact the presence of a cystic tendency may be difficult to recognize because the osteofibrosis often obliterates the cysts even if they are potentially present. The disease is nearly always found in young people.

It may be of interest to note that the cases forming the basis for this discussion were only 5 in number, but they had many points in common. The body chemistry was apparently normal as far as could be determined by the usual tests, which have always seemed to me to leave a lot to be desired. In all 5 cases one of the first objective symptoms to be noted was local tenderness and tumefaction. One case complained of "dizzy spells" and one-sided

headaches. Two cases gave histories of trauma to the involved area, preceding by an indefinite time the onset of the symptoms. In one case there was a feeling of general malaise and dull generalized headaches.

When osteitis fibrosa occurs in the skull, the disease is most apt to attack the bones of membranous origin which include the vault. The lesions originate usually in the diploe, and produce osteolysis of the outer table before involving the inner table. Usually there is some tumefaction in which giant cells predominate, and it is this tumor formation that may bulge inward giving rise to symptoms of localized cerebral pressure. The disease is no respecter of suture lines, and may spread widely, which is not uncommon, or it may remain as a small localized lesion, but the tendency is toward gradual enlargement.

The case illustrated in Figure 2 was the first of the series, and there was considerable discussion as to what the diagnosis might be, so in order to be sure, a biopsy was done and the microscopic findings were reported as follows by Dr. Arthur Purdy Stout:

- (1) The outer table shows an intertrabecular fibrosis in part of the bone while the rest of it shows normal bone and bone marrow.
- (2) The specimen removed from beneath the outer table shows that the cancellous bone has had its trabeculae greatly widened by the growth of exceedingly dense and relatively avascular fibrous tissue. The bone trabeculae in this area appear inactive, showing no evidence of proliferation nor of erosion. This zone merges at one end with a more vascular, granulomatous tissue in which there are a large number of multinucleated phagocytic giant cells, some of which are vacuolated. In this tissue there is no bone or osteoid found. This

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Fig. 1. Osteofibroma. The lesion involves the superior portion of the left parietal bone. The bone is thickened and appears mottled, but there is no increased vascularity.

is the tissue which formed the lining of the hemorrhage-filled cavity.

(3) The wall of the hematoma consists of a granulomatous tissue with large numbers of multinucleated phagocytic giant cells. Adherent to the inner surface is some partly organized blood clot.

This lesion is similar to that found in the majority of cases of osteitis fibrosa. The intertrabecular fibrosis extends outward from the cystic area somewhat further than in the usual case, although not very much further. This cannot be regarded as sufficient to invalidate the diagnosis. It is quite usual to find the periphery of the lesion almost exclusively fibrous while the portion of it which comes into contact with the blood clot is vascular, granulomatous, and contains large numbers of multinucleated giant phagocytes. In none of the sections is there any evidence of bone proliferation.

Diagnosis: Osteitis fibrosa cystica of frontal and parietal bones.

In discussing with Dr. Stout the characteristics of this particular form of osteitis fibrosa cystica, which might be termed osteitis fibrosa localisata, the question arose as to whether or not there was any difference between this local manifestation and

the generalized form of the disease caused by parathyroidal overactivity. He was strongly of the opinion that microscopically the conditions were identical, but agreed that the localized form as seen in the calvarium might be termed an osteofibroma so as not to confuse the two clinically and roentgenologically.

Hyperparathyroidism, when caused by a tumor of the parathyroids, produces bone changes which Dr. Stout feels cannot be differentiated microscopically, as a rule, from the changes of osteitis fibrosa cystica. This, in spite of the fact that hyperparathyroidism when seen in the skull is quite different roentgenologically (see Fig. 7). It is also of interest to note that if the parathyroid tumor is completely removed, the bones of the skull rapidly tend to revert to a comparatively normal appearance which seems to indicate that the bone structure is not permanently disoriented, although the bone in the presence of an osteofibroma is permanently changed. Evidently the bone reaction up to a certain point is quite similar in the two conditions, but tends to be more profound in the case of osteitis fibrosa.



Fig. 2. Osteofibroma. The lesion is widespread through the frontal and anterior parietal regions. The defect in the extreme frontal region is the result of a biopsy.

In making a differential diagnosis of an osteofibroma, one must first exclude the possibility of the bone changes being caused by a meningiotheliomatous or "en plaque" type of meningioma. This may be difficult at times but usually it is possible to see in good stereoscopic films that there is no spiculation which is likely to be present with a meningioma, and also there will be no alteration in the vascularity. As a rule, the symptoms would be much

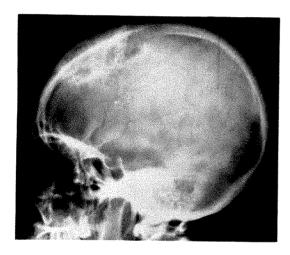


Fig. 3. Osteofibroma. The lesion is frontal and has produced some fusiform swelling of the outer table.

less marked with an osteofibroma than they would be in the presence of a meningioma; and in its early stages, the meningioma would involve the inner table before the outer table would show any changes.

Metastatic malignant tumors at times may simulate the roentgenographic bone changes of an osteofibroma. Lesions caused by metastatic tumors are almost always multiple and chiefly osteolytic. The bone structure is actually destroyed and there is little or no attempt at repair, which is not usual with an osteofibroma. The history of the case would help to rule out metastatic disease.

Osteomyelitis, particularly the luetic variety, might produce a lesion almost identical with an osteofibroma. In fact, the history and clinical findings might be necessary to differentiate between these

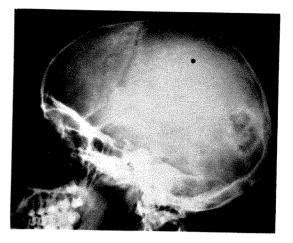


Fig. 4. Osteofibroma, A small lesion appears in the occipitoparietal region.

two conditions. The lesions of osteomyelitis are not apt to produce any tumefaction except the luetic type which often is accompanied by an overlying gumma. Osteomyelitic changes are prone to stop at suture lines but at times they will follow along the suture lines particularly in children. Osteolysis is often predominant, and frequently about the edges there will be evidence of bone repair, particularly if the

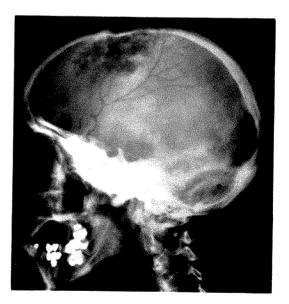


Fig. 5. Osteofibroma, A frontoparietal lesion appears which is more predominantly osteolytic than is usually seen. Note the involvement of the outer table,

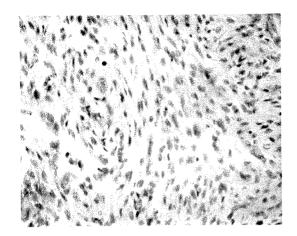


Fig. 6. Photomicrograph (×700) of biopsy section taken from case illustrated in Figure 2.

infection is old. Here again, the history will play an important rôle in the final differentiation.

A cavernous hemangioma of bone can produce a localized skull lesion. Such a lesion almost always gives rise to bony spiculation which will be of a radiating somewhat perpendicular type interspersed with myriads of small areas of decreased density not unlike numerous little insect eyes peering out from indentations in the bone. Such a change would not be caused by an osteofibroma.

A localized early Paget's disease could roughly simulate an osteofibroma. In fact the two diseases have many factors in common. Paget's disease is apt to be more widely spread and not so clearly localized. In the early stages these two conditions might be indistinguishable, provided the Paget's disease was markedly localized. Later on in the course of Paget's disease, the thickening of the calvarium and the tendency toward irregular osteoporosis would easily differentiate the lesion from that produced by an osteofibroma.

In brief, the roentgenographic appearance of an osteofibroma in the skull is characterized by an almost complete disorientation of bone structure, with no hypervascularity, no evidence of bone repair, some osteolysis, thickening of a fusiform type mostly through the outer table,

and no spiculation. The history is usually unimpressive, and consists essentially of local tenderness with some indefinite form of mild headache.

The treatment of an osteofibroma is chiefly surgical. Radiation in fairly large, well filtered doses may be tried. The lesion progresses very slowly, so that no harm

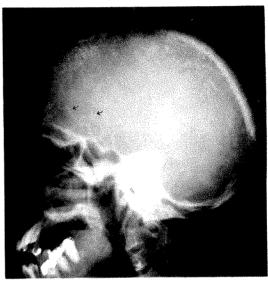


Fig. 7. Hyperparathyroidism. The granular appearance of the bones is almost characteristic of this disease. It is interesting to note that in this case the blood vessels of the meninges are calcified (arrows).

would be expected to follow a sufficient delay to give radiation a trial. Usually, however, radiotherapy will prove disappointing.

#### REFERENCES

- I. Arons, I. Ossifying fibroma of the maxillary sinus; report of case successfully treated with irradiation. Am. J. Cancer, 1937, 29, 551-555.
- 2. Figi, A. Multiple fibro-osteomas of superior maxilla. S. Clin. North America, 1933, 13, 878-880.
- 3. Geschickter, C. F., and Copeland, M. M. Tumors of Bone. Second edition. American Journal of Cancer, New York, 1936, p. 681.
- HASLHOFER, L. Gutartige Riesenzellentumoren der Knochen und segenannte Knochensystem. In: Henke and Lubarsch, Handbuch d. spez. path. Anatomie und Histologie. 1937, o. pt. 3, pp. 485, 494.

- 5. Hummel, R. Die Behandlung der solitären Riesenzellengeschwülste. Röntgenpraxis, 1932, 4, 545-564.
- Jentzer, A. Ostéofibrome douloureux du maxillaire supérieur gauche. Schweiz. med. Wehnschr., 1935, 65, 101-103.
- 7. Kindler, W. Ostitis fibrosa des Gesichtsschädels, zur Diagnose und Behandlung. Ztschr. f. Laryng., Rhin., Otol., 1934, 25, 54-59.
- 8. KIRKLIN, B. R., and Moore, C. Roentgenological manifestations of giant-cell tumor. Am. J. Roentgenol. & Rad. Therapy, 1932, 28, 145-150.
- 9. Koblin, H. A. Zur Ursache der symmetrischen Schwellungen der Zahnfortsätze. Virchow's Arch. f. path. Anat., 1932, 283, 631-652.
- 10. Landais, P. Tumeurs à myéloplaxes des maxillaires et infection dentaire périapicale. Rev. de stomatol., 1933, 35, 199-210.
- 11. Meadows, J. A., and Kesmodel, K. F. Roentgen diagnosis and treatment of benign giant cell tumor of bone. South. M. J., 1938, 31, 148-153.
- 12. MÖLLER, P. F. Zwei Fälle von Riesenzelltumoren im Os occipitale. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1936, 53, 465-470.
- 13. MOULONGUET, P. Tumeur à myéloplaxes. In:
  Ombrédanne and Mathieu, Traité de chirurgie
  orthopédique, 1937, 1, 427. ("Sur les os du
  crâne la lésion paraît être exceptionelle," p.
  429.)

- 14. PFAHLER, G. E., and PARRY, L. D. Treatment of giant-cell bone tumors by roentgen irradiation. Am. J. ROENTGENOL. & RAD. THERAPY, 1932, 28, 151-166.
- 15. Phemister, D. B., and Grimson, K. S. Fibrous osteoma of the jaws. Ann. Surg., 1937, 105, 564-583.
- 16. RAMADIER, J. A., and TOURNAY, A. Une observation de tumeur à myéloplaxes du Rocher. Rev. d'oto-neuro-opht., 1937, 15, 29-32.
- 17. RINGERTZ, N. Pathology of malignant tumors arising in nasal and paranasal cavities and maxilla. *Acta oto-laryng.*, suppl. 27, 1938, 190–194; 205–208; 372–374; 375–376.
- 18. Sabrazès, J. E., Jeanneney, G. and Mathey-Cornat, P. Les tumeurs des os. Masson et Cie, Paris, 1932, p. 162.
- SJÖBERG, ARNE. On the clinical treatment of osteoma of maxillary sinus. *Acta oto-laryng.*, 1935, 23, 157-166.
- SNYDER, H. L. Giant cell tumor; report of case involving mastoid. J. Kansas M. Soc., 1935, 36, 189-192.
- 21. Wattles, M. Case of benign giant cell tumor of ethmoid labyrinth with review of the literature. Ann. Otol., Rhin. & Laryng., 1937, 46, 212-222.
- 22. WIEDER, H. S. Case of giant cell tumor of septum nasi. *Laryngoscope*, 1932, 42, 786-787.



# THE EFFECT OF PEPTIC ULCER IN CHOLECYSTOGRAPHY

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IT IS believed by many authorities that peptic ulcer, because of the high acidity associated with it, is an important factor in many cases of non-filling of the gallbladder in cholecystography. Brailsford,1 Robins and Goldberg, Leb, and others, emphasized the fact that non-filling of the gallbladder often occurs in cases of duodenal ulceration. Friedenwald, Feldman and Kearney,4 in their investigation of the effect of gastric acidity on gallbladder visualization, found that the gallbladder shadows are often not as dense as those obtained in cases which have a normal acidity. In a series of cases of duodenal ulcer, with high gastric acidities, in which oral cholecystographic examinations were made, we4 did not observe a single instance in which failure to visualize the gallbladder could be definitely attributed to high gastric acidity. These results were undoubtedly due to the large dosage of dye which had been administered. Boyden and Berman observed a normal visualization of the gallbladder in 30 out of 33 cases (90.9 per cent) of peptic ulcer. We had believed that non-filling of the gallbladder, due to peptic ulceration, occasionally occurs, but is an uncommon observation.

Since there are many controversial opinions regarding the effect of peptic ulcer on cholecystography, a series of 115 consecutive cases of peptic ulcer was studied to determine the effect of peptic ulcer on the visualization of the gallbladder.

It is a definitely known fact that exceedingly high acidities of the stomach, with lowering of the pH of the intestinal content, plays a distinct rôle in changing the soluble tetraiodophenolphthalein dye into its insoluble compound. In cases of peptic ulcer, the density of the vesicle shadow is often reduced to a marked de-

gree. It has been our experience that when a small dosage of tetraiodophenolphthalein was administered, non-filling of the gall-bladder occasionally occurred. This could be overcome in many instances if an additional dose of dye were given immediately. When the larger dosage of the dye was administered in peptic ulcer cases, cholecystography ordinarily yielded a normal gall-bladder shadow in the majority of cases.

In our series of 115 cases of peptic ulcer, 112 were duodenal and 3 gastric. These cases were carefully analyzed following cholecystography to study the effect of peptic ulceration and its associated high gastric acidity upon visualization of the gallbladder. Of the 115 cases, a satisfactory gallbladder shadow of normal density was obtained in 101, or 87.7 per cent. In 9, there were poor filling or faint shadows, and in 5, non-filling of the gallbladder. It is interesting to note that in the 3 cases of gastric ulceration, 2 filled well, and in the other there was a non-filling gallbladder. Gallstones were found in 6 instances, 4 of which revealed a normal filling and in 2 a poor filling gallbladder.

A study of the emptying of the gallbladder following a fat meal, consisting of two eggs and a glass of milk, was made to determine the effect of peptic ulcer on the contraction of the vesicle. Examinations were made from thirty to sixty minutes after the fat meal. Bronner<sup>6</sup> and Boyden and Berman, point out that the rate of evacuation of the gallbladder is considerably accelerated in cases of peptic ulcer. In our study of gallbladder emptying, the size of the original filled vesicle shadow was. taken as a standard, and the contraction was considered normal in those cases which contracted to less than half the original size; poor or sluggish confraction, in

those which were only slightly reduced in size, and non-contraction, in those which did not contract at all. In 110 visualized gallbladders, 80, or 72.7 per cent, responded normally following the fat meal. In 21 instances, or 19 per cent, there was a sluggish contraction, and in 9, or 8 per cent, no change in the size of the vesicle could be observed. In the 9 cases that failed to respond to the fat meal, 4 in the original films presented a faint shadow.

These studies were made from clinical and roentgenological observations in routine investigations of 115 consecutive cases of peptic ulcer. There were few surgical and no autopsy studies to confirm our findings. In the 9 cases which showed a poor filling or faint shadow of the gallbladder, only 2 were pathologically accounted for by the presence of gallstones: the remaining 7 cases and the 5 cases of nonfilling gallbladders represent 10.4 per cent of the series which revealed abnormal cholecystographic findings. This percentage of abnormal cholecystograms seems rather high. In these cases there is some question of doubt whether or not the abnormal findings represent a pathological gallbladder or changes due to peptic ulceration. However, we are inclined to believe that some of these cases may be due to a pathological condition of the biliary tract, but many are probably due to peptic ulcer and the coexisting high gastric acidity. In those instances in which an abnormal cholecystographic finding occurs, the test can be repeated by utilizing the intravenous route to further support the observations made by the oral method. Even by the former procedure, the gallbladder may yield an abnormal cholecystographic test, as pointed out by Leb.3 He performed intravenous cholecystography in 100 patients with duodenal ulcer and found that 26 per cent of organically healthy gallbladders failed to fill. These roentgen findings were confirmed in 25 cases which came to operation. The exact mechanism which produces a non-filling

gallbladder by the intravenous method in cases of peptic ulceration has not been definitely explained. It is likely that dyskinesia of the gallbladder plays an important factor in these cases.

It is noteworthy to point out that dyskinetic changes of the gallbladder are commonly observed in the cholecystographic test in cases of peptic ulcer. In our series of 110 cases of filled gallbladders, 27.3 per cent revealed a sluggish or non-contracting gallbladder following a fat meal. Leb likewise directed attention to the fact that in many cases which showed signs of dyskinesia, the fat meal led to an accelerated or retarded evacuation of the gallbladder. He attributed this behavior of the gallbladder in cases of duodenal ulcer to the result of nervous irritative processes. Bronner and Boyden and Berman found an accelerated evacuation of the vesicle in peptic ulcer.

#### SUMMARY

Cholecystographic studies made in 115 cases of peptic ulcer revealed that the administration of a large dosage of dye usually tends to produce a more constant vesicle shadow of normal density than a smaller dosage. The larger dosage also probably reduces the number of cases of abnormal cholecystograms in peptic ulcer. Although we had believed that peptic ulcer had little practical significance on the filling or non-filling of the normal gallbladder. our observations reveal a rather high percentage (10.4 per cent) of abnormal filling in cases of peptic ulcer. In peptic ulcer there is frequently observed a dyskinesia of the gallbladder, resulting in its acceleration or retardation of emptying. In our series of cases of peptic ulcer, 27.3 per cent yielded a sluggish or non-contracting gallbladder. Of 115 cases of peptic ulcer, 6, or 5.2 per cent, were associated with gallstones. This study corroborates the general roentgenologic belief that peptic ulcer is undoubtedly responsible for many cases of non-filling of the gallbladder.

#### REFERENCES

- 1. Brailsford, J. F. Cholecystography. Lancet,
- 1932, 2, 566-569. 2. Robins, S. A., and Goldberg, B. I. Cholecystography; examination of 1000 cases by oral method. New England J. Med., 1929, 201, 114.
- 3. Leb, A. Experimental contribution to the cholecystographic non-filling of the gallbladder in duodenal ulcer. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1931, 44, 16-27.
- 4. FRIEDENWALD, J., FELDMAN, M., and KEARNEY, F. X. Experimental studies in cholecystog- . raphy. Radiology, 1927, 9, 68-72.
- 5. BOYDEN, E. A., and BERMAN, T. M. Evacuation of the gallbladder in peptic ulcer patients. Radiology, 1937, 28, 273-282.
- 6. Bronner, H. Die cholezystographische Motilitätsprüfung der Gallenblase und ihre Ergebnisse. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1929, 39, 23-76.



## GASTRIC NEURINOMA

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#### HISTORICAL INTRODUCTION

T HAS only been within the last decade that attention has been directed to the occurrence of visceral neurinomas. Previously these tumors had only been described in the region of the central nervous system and peripheral nerves and had been designated as neurofibromas and peripheral gliomas. Since the time of Verocay's18 work on the histology of these tumors they have been segregated as a distinct pathological entity and within the past decade the number of reported cases in the literature have become increasingly more frequent. Undoubtedly many cases of gastrointestinal neurinomas had previously been erroneously classed among the ganglioneuromas, neurofibromas, and sarcomas.

The very complex subject of tumors of nervous origin is made even more confusing by the large and varying nomenclature. We are dealing with a group of tumors which histologically have much in common and in spite of the varying terminology are closely interrelated. The French school under Masson<sup>12</sup> prefer the term gastric gliomas or schwannomas believing that they are ectodermal in origin and arise from the cells of the sheath of Schwann, while in the English literature there is shown a preference for the term perineurial fibroma or fibroblastoma.

#### INCIDENCE

Among all the benign tumors of the stomach the neurinoma is without doubt the rarest, although the neuromuscular apparatus of the stomach wall, especially in the lesser curvature, is abundant in nervous tissue. In a study of 2,168 neoplasms of the stomach by Eusterman and Senty, only 27, or 1.3 per cent, were benign among which there was not one case of neuri-

noma. Minnes and Geschickter,<sup>14</sup> in a review of 50 cases of benign tumors of the stomach collected at Johns Hopkins, make no mention of gastric neurinoma. Balfour and Henderson<sup>3</sup> of the Mayo Clinic published 58 cases of benign tumors of the stomach without one neurinoma.

#### ETIOLOGY

These tumors are all thought to arise from the specialized investment which separates and insulates nervous tissue from the surrounding structures. In the stomach wall are to be found the same nerve plexuses which are present in the wall of the intestine, namely, the submucous plexus of Meissner and the myenteric plexus of Auerbach. The question of the etiology of gastric neurinomas will not be considered in detail as this represents a highly controversial subject. Masson<sup>12</sup> is a strong advocate of the neuro-ectodermal origin from the schwannian syncytium as opposed to the idea that these tumors are to be regarded as fibroblastomas arising from the perineurium or connective sheath of nerves, therefore à perineurial fibroblastoma.

Enormous proliferative changes in the nerves of the stomach wall in the neighborhood of inflamed gastric mucosa and gastric ulcers have been described which are thought to be the result of progressive inflammatory antecedents. These have been studied by Masson<sup>13</sup> in the walls of obliterated appendices and by Askanazy1 in the wall of the stomach adjacent to gastric ulcers. The latter found in the cicatricial areas of gastric ulcers a pathological abundance of nerve fasciculi. This may reach considerable proportions, as in the case cited by Dupuy,8 in which pathological examination of the stomach of a case of attempted suicide by means of hydrochloric acid ingestion showed a diffuse intramuscuto each other and an intervening fibrillar palisade."

IANUARY, 1940

lar neuroma, resulting in the formation of plexiform nerve fibers and ganglia accompanying an inflammatory lesion of the mucosa and submucosa. The relationship between these nervous proliferations and true benign gastric new growths of nervous origin is highly speculative.

These tumors are mostly benign although Carnot's case showed cell proliferation of a sarcomatous character. Denecke reports 2 cases of metastasizing neurinoma of the gastrointestinal tract, one occurring in the duodenum as a pedunculated tumor, the other a lobulated endogastric tumor arising from the greater curvature of the stomach. Both cases at autopsy showed extensive liver metastases.

#### PATHOLOGY

## CLINICAL MANIFESTATIONS

The benign tumors of the stomach with nervous elements have been divided into three categories: (1) ganglioneuromas, (2) neurofibromas, and (3) neurinomas or schwannomas. It is with the last group that we are here primarily concerned.

There are no characteristic clinical signs associated with gastric neurinomas which would not be manifested by any gastric lesion either inflammatory or new growth. Hemorrhage occurs in a surprisingly large number of the cases where ulceration of the tumor is present. Hortolomei and Burghele<sup>10</sup> report a case with massive severe hematemesis without previous gastric manifestations in the history. The frequent occurrence on the posterior wall of the stomach may favor hemorrhage either in the form of melena or hematemesis.

These tumors are grossly soft, elastic, well circumscribed, spherical, often lobulated and pedunculated, although they may be attached to the stomach wall by a broad base. They are said to occur most frequently on the posterior wall of the stomach, frequently near the lesser curvature. They are usually single, covered by mucous membrane which is very vascular and may be thickened, and may or may not be ulcerated. Frequently, because of their size and location, they interfere with the circulation to the overlying mucosa resulting in necrosis and ulceration. The presence of ulceration accounts for the very characteristic "en face" niche so frequently seen on the roentgenogram.

Rarely is a mass to be palpated, as in the case reported by Barber,4 in which the patient noted a large, freely movable, painless mass in the upper quadrant of the abdomen, which showed no change in size and remained symptomless for nine years. Iceton, Poate and Tebbutt<sup>11</sup> report a case with pain across the upper abdomen, vomiting, and constipation. Death resulted from collapse following repeated severe melena. At autopsy the tumor which was attached to the greater curvature of the stomach had prolapsed through the pylorus producing gastric intussusception. In-Ritter's16 case the rhythmically recurring boring pain in the epigastrium, regularly related to meals, unaffected by diet and producing severe night pain, strongly simulated those of an ulcer, with a suggestion of possible perforation.

Microscopically the picture is very characteristic in the palisade arrangement of the elongated nuclei. According to Masson12 "the specific cells of this tumor are connected in a syncytium like Schwann cells; they possess elongated nuclei and they are grouped in networks, in bundles and in palisades. These latter structures are pathognomonic. The palisades consist of oval nuclei aligned in the same transverse plane 'like staves on a barrel' (Verocay). On each side of this nuclear palisade, or on one side only, there is a fibrillar band parallel to it. The fibrils are oriented like the nuclei, running perpendicular to the nuclear band. Thus a palisade system is formed by two nuclear palisades parallel

#### ROENTGEN DIAGNOSIS

The diagnosis is best made preopera-

tively by means of the roentgen examination from which, in typical cases, the exact diagnosis can be strongly suspected. Characteristically it presents an oval to round smoothly outlined defect with an "en face" niche. The defect is usually on the gastric walls leaving the curvatures free and regular. The smooth, well circumscribed appearance situated away from the gastric curvatures lends weight to the diagnosis of a benign tumor. Retention is not present unless the tumor is close enough to the pylorus to produce obstruction by prolapse. Peristalsis is undisturbed and a study of the mucous membrane pattern in the region of the tumor shows neither the radiation of the rugal folds suggestive of an ulcer nor the sudden termination as in malignancy. The presence of several irregular flecks of contrast material would indicate the existence of several ulcerations and would suggest the roentgen image of a degenerating malignancy.

#### REPORT OF CASE

A. P. (No. 94134), female, white, married, aged sixty, admitted May 10, 1938, with the chief complaint of having vomited blood the morning of admission and the night previous. The patient has had no previous admissions. The onset of the present illness began approximately four and one-half years ago at which time the patient began to have occasional pains in the epigastrium usually several hours after meals and relieved by alkalis. These episodes would occur two or three times weekly though with no great regularity and were occasionally accompanied by nausea and vomiting. In June, 1934, the patient had an attack of hematemesis following an exacerbation of her gastric distress and states that she vomited about a pint of dark blood. She remained in bed at that time for about three weeks and was placed on a soft diet by her physician. After her recovery the patient discontinued her diet and had a recurrence of hematemesis three years ago, following which she remained in bed for about a week. For the past three years there has been no repetition of the hematemesis although the gastric pains have persisted with the same regularity and with no increase in severity. The pains may occur two or three

times weekly and then may be absent for two or three weeks.

One week before admission the patient began to have the gastric pains several times a day accompanied by nausea. The pain occurs usually about two hours after meals, starts in the epigastrium, has apparently not been severe, and seems to radiate downward. The evening before admission the patient had a fairly severe pain in her epigastrium and felt nauseated. A short time later she vomited about one pint of coffee ground vomitus and felt dizzy and weak. On the morning of admission the patient had several tarry stools and was seized with a moderately severe pain in the epigastrium and became nauseated and vomited about one pint of bright red blood.

The physical examination revealed some tenderness in the epigastrium and around the umbilicus. A few cardiac extrasystoles were noted. The immediate treatment consisted of blood transfusions, intravenous glucose, and the Meulengracht diet, to which the patient readily responded. A gastroscopic examination was done which revealed a deep ulcerative lesion at about the angulus on the lesser curvature of the stomach. The lesion appeared sharply defined and its upper border was about 9 cm. from the cardiac end. No evidence of gastritis elsewhere in the stomach. The gastroscopic impression was malignant ulcer (Schindler Type 2), operable.

Gastrointestinal series showed an "en face" ulcer niche measuring about 2 cm. in diameter on the posterior wall of the stomach near the lesser curvature in the middle third of the stomach (Fig. 1). There was some tenderness over the ulcer but no mass could be palpated through the abdominal wall in this region. The blood Kahn reaction was negative. Blood urea determinations showed progressive fall from 29 mg. per 100 cc. on May 10 to 15 mg. per 100 cc. on May 13.

The patient was operated on May 26 and a sleeve resection of the ulcer with wide margins was done with end-to-end anastomosis. Exploration at the time of operation revealed a hard crater-like ulcer at the junction of the upper and middle thirds of the stomach near the lesser curvature. The ulcer and surrounding reaction was about  $1\frac{1}{2}$  inches in diameter and the crater was about  $\frac{3}{4}$  inch deep. Complete inspection of the regional glands showed no evidence of metastasis.



Fig. 1. Roentgenogram made in the exaggerated left anterior oblique position showing large "en face" niche, indicated by arrow.

Pathological Report. Dr. Ralph H. Fuller. Buried in the wall of the stomach, overlying a line of omental attachment, is an encapsulated, spheroid, solid tissue mass measuring 3 cm. in diameter (Fig. 2). The substance of the tumor is firm, gray and homogeneous. The cut surface does not present the characteristically whorled appearance of interlacing bundles of fibers cut in various planes so commonly seen in myomas and fibromas. There is no apparent displacement of serosa or serosal supporting tissue by





Fig. 2. Specimen of stomach wall removed at operation showing spheroid, solid tissue mass, bulging into the lumen of the stomach with central ulceration.

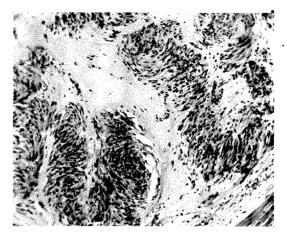


Fig. 3. Low magnification showing hyaline ground substance and bands of cellularity with whorls, eddies and palisading nuclei. Hematoxylin-eosin stain.

the mass which bulges into the lumen of the stomach producing a smoothly rounded hillock having a broad circular base. The gastric mucosa, only loosely attached to the capsule of the tumor mass, is everywhere of normal thinness and intact save at the apex of the hillock. Here there is an ulcer measuring 1 by 2 cm., without evidence of epithelial overgrowth at the ulcer margins. The ulcer crater perforates the capsule of the tumor and penetrates to a depth of 2 cm. in the tumor mass.

Microscopically the tumor is composed of hyaline or loose reticular substance supporting ribbon-like ranks of palisaded elongated nuclei. The ranks of nuclei appear irregularly to branch and anastomose presenting numerous whorls and eddies (Fig. 3). In the hyaline sup-

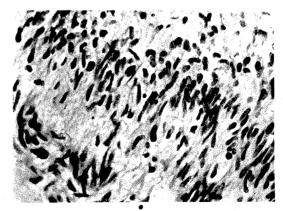


Fig. 4. High magnification of a cellular field. Hematoxylin-eosin stain.

porting substance there are scattered small areas in which calcium salts have been precipitated. The relatively avascular tumor mass is perfectly encapsulated. There is a narrow superficial zone of necrosis and acute inflammatory reaction in the floor of the ulcer.

Diagnosis. Benign neurinoma (perineurial fibroma or schwannoma) of the stomach.

#### SUMMARY

- (1) Increasing familiarity with and more accurate interpretation of the histologic findings in gastric neurinomas has resulted in a marked increase in the number of cases reported in the literature of the past decade.
- (2) The characteristic histological findings of elongated nuclei with a palisade formation, "like the staves of a barrel" grouped in networks, and bundles and presenting numerous whorls and eddies is emphasized.
- (3) Hemorrhage, either in the form of melena or hematemesis, is a common clinical finding in gastric neurinomas.
- (4) The roentgen findings may be sufficiently characteristic to permit of an accurate preoperative diagnosis. Classically this is an oval to round, smoothly outlined defect with an "en face" niche, usually located on the posterior wall of the stomach, leaving the curvatures regular and undisturbed.
- (5) Most cases of gastric neurinomas are benign although malignant transformation has been recorded.

I wish to make grateful acknowledgment of the kindness extended me by Drs. Mont R. Reid and Leon Schiff of the staff of the Cincinnati General Hospital for making the clinical record of this case available to me, and to Dr. H. G. Reineke for his guidance and advice in the preparation of the manuscript.

#### REFERENCES

 ASKANAZY, M. Ueber Nervenwucherungen im chronischen Magengeschwur und über ein Magenherzgeschwur. Schweiz. med. Wehnschr., 1926, 56, 661-665.

- 2. Askanazy, M. Quoted by Dupuy, ref. 8.
- 3. Balfour, D. C., and Henderson, E. F. Benign tumors of the stomach. *Ann. Surg.*, 1927, 85, 354-359.
- 4. BARBER, T. H. T. Large sub-mucous tumour of the stomach (fibroneuroma or schwannoma). Tr. Med. Soc., London, 1932, 55, 95-98.
- BOYD, W. Surgical Pathology. Third edition. W. B. Saunders Co., Philadelphia, 1933, p. 961.
- 6. CARNOT, P. Tumeurs sous-muqueuses de l'estomac (Schwannomes). Ann. de méd. et de chir., 1928-1929, 1, 37-49.
- 7. Denecke, K. Ueber zwei Fälle von metastasirenden Neurinomen des Magendarmkanals. Beitr. z. path. Anat. u. z. allg. Path., 1932, 89, 242-248.
- 8. Dupuy, M. Neuroma of the gastric walls. *Internat. Clin.*, 1925, 4, 164-170.
- 9. Eusterman, G. B., and Senty, E. G. Benign tumors of the stomach. Surg., Gynec. & Obst., 1922, 34, 5-15.
- HORTOLOMEI, N., and BURGHELE, T. Kasuistischer Beitrag zur Frage der Neurinome des Magens. Zentralbl. f. Chir., 1937, 64, 2822–2825.
- 11. ICETON, S. G., POATE, H. R. G., and TEBBUTT, A. H. Gastric intussusception in an adult due to a rare tumour. *Med. J. Australia*, 1931, 1, 82-84.
- 12. Masson, P. Experimental and spontaneous schwannomas (peripheral gliomas). Am. J. Path., 1932, 8, 367-388; 389-416.
- Masson, P. Les nevromes sympathiques de l'appendicite obliterante. Lyon chir., 1921, 17, 281-299.
- 14. MINNES, J. F., and GESCHICKTER, C. F. Benign tumors of the stomach. Am. J. Cancer, 1936, 28, 136-149.
- MOORE, A. B. Roentgenologic study of benign tumors of the stomach. Am. J. ROENTGENOL. & RAD. THERAPY, 1924, 77, 61-66.
- RITTER, A. Beitrag zur Kenntnis des Neurinoms des Magens. Schweiz. med. Wchnschr., 1931, 61, 1201–1204.
- 17. VAN GELDEREN, C. Ueber Neurinome (Gliome) und andere gutartige Geschwülste des Magens. Deutsche Ztschr. f. Chir., 1938, 249, 603-615.
- Verocay, J. Zur Kenntnis der Neurofibrome. Beitr. z. path. Anat. u. z. allg. Path., 1910, 48, 1-69.
- 19. Waters, C. A., and Kaplan, I. I., Editors. Yearbook of Radiology. Yearbook Publishers, Inc., Chicago, 1937, p. 184.



## CONGENITAL SYNOSTOSIS OF THE CERVICO-THORACIC VERTEBRAE (THE KLIPPEL-FEIL SYNDROME)\*

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HUTCHINSON<sup>24</sup> in 1894 described an anatomical specimen in which there was fusion of the vertebral bodies and a cleft of the arches from the third to the sixth cervical vertebra. The first clinical reference to this condition was the presentation by Clarke<sup>7</sup> in 1906.

The first comprehensive report in the literature of congenital synostosis of the cervical spine appeared in 1912 by Klippel and Feil. 28,29 This was the case of a male, aged forty-six, who died of pneumonia, and at necropsy showed complete fusion of the cervical spine and posterior spina bifida occulta. This condition has since been commonly designated as the "Klippel-Feil syndrome." It is referred to by the French as "l'homme sans cou" and by the Germans as "Kurzhals."

In 1919 Feil collected the records of 14 cases and by 1925 he and his collaborators<sup>9-16</sup> contributed 14 articles on the subject. A review of the literature shows a predominance of European reports. There are at least eighty-three articles reporting 133 cases. The noteworthy contributions are by Kallius,26 and by Bertolotti,4 who reported 18 cases and 9 cases respectively. Fourteen articles have appeared in the English and American literature reporting 28 cases. Meisinbach's report in 1912 was the first to appear in the American literature. Since then the following have contributed articles on the subject: Noble and Frawley, 35 Greig, 21 and Willard and Nicholson.44 Each reported 2 cases. Bauman3 and Mitchell<sup>33</sup> have each reported 6 cases. The remaining presentations are individual case reports. 18,36,37,38,41,43

American and English anato-

mists<sup>6,19,20,32,34,42</sup> in six articles reported 30 specimens of anomalous and congenitally deformed cervical spines. One such article<sup>8</sup> appeared in the French literature. This would seem to suggest that much of the clinical material observed has not been reported and that the condition, though infrequent, is probably not rare.

#### EMBRYOLOGIC CONSIDERATION<sup>27</sup>

The notochord, the most primitive form of axial support, appears in the human embryo from the third to the fifth week. Three stages are noted in the evolution of the spinal column: (1) Primitive segmentation (somites), (2) the cartilaginous stage in which the cells of the mesenchyme become modified into cartilage forming cells and (3) the final stage where cartilage is replaced by bone. These changes occur in rapid succession in the human embryo during the second month of gestation.

The neural tube is formed (third week) from a strip of ectoderm or epiblast from along the median dorsal line and ventral to it, the notochord in like manner from the archenteron. The paraxial mesoderm on either side becomes segmented. These segments, known as somites or protovertebrae, are separated from each other by septa. The notochord begins to disappear in the second month due to the action of the bodies of the vertebrae and parachordal cartilage which form about and constrict it. It only persists as the nucleus pulposus in the disc between the vertebral bodies.

In the membranous stage (fifth and sixth weeks) the vertebrae consist of a centrum surrounding the notochord and a horseshoe-shaped vertebral bow, the latter consisting of a right and left limb which become corresponding parts of the neural vertebral arch. These are united anterior to the centrum by the hypochordal bow. During the cartilaginous stage (sixth week), the entire fibrous base is transformed

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into cartilage and three centers of chondrification appear, one each for the neural arch, the costal process and the centrum. The vertebral bodies are formed opposite each intersegmental septum, and hence, each centrum is the product of two somites. At the fourth month the lateral cartilaginous limbs meet dorsal to the neural canal and failure to do so results in spina bifida.

Two centers of ossification appear and fuse in the centrum in the bony stage (seventh week). One appears in each of the two limbs of the neural arch and unite at the fourth or fifth year. The body of the vertebra is formed from the centrum and the basal part of the neural arch. The neural ossifications fuse posteriorly in the first year and the spinous processes, transverse processes and ribs are formed by outgrowths of cartilage into the septa between the somites. The costal processes fuse with the transverse processes except in the dorsal region where they remain as separate elements.

The atlas represents the completed bow of the first cervical vertebra. Its body fuses with the body of the second to form the odontoid process of the axis. The occipital or posterior part of the skull represents at least three united vertebrae. Very rarely the last of these may partly assume a vertebral form. It is not rare to see the first cervical vertebra partly fused with the occipital bone. This represents a tendency to add a fourth vertebra to the occipital series. In the cervical vertebrae the anterior part of the transverse process represents a costal process, but only in the sixth and seventh is this process formed by a separate ossification center which is usually vestigial and may form a rudimentary or fully developed rib.

Since a vertebra has its own potentiality and may assume the characteristics of the segment above or below it, such irregularities are classed as "normal or functional." During the period of segmentation the embryo may be subjected to injurious conditions and "abnormal or pathological" peculiarities may be produced. Segments may separate irregularly so that ribs or vertebrae become fused, or hemivertebrae occur. Associated anomalies in the other systems are not infrequent. Figure 1 depicts the spinal column and the costal series of a fetus illustrating marked irregularity in segmentation.

#### ETIOLOGY

A congenital synostosis of the cervical spine (Klippel-Feil syndrome) is therefore

probably due to the irregular segmentation of the spine occurring in the early weeks of fetal life. Such disturbances of normal development are not to be regarded as regressive or progressive tendencies in phylogeny, but are rather the result of morbid conditions in the parent interfering with the normal fetal development.

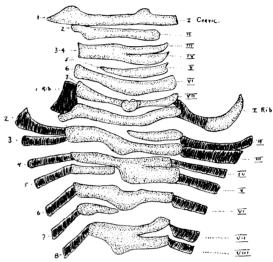


Fig. 1. Cervical and dorsal parts of the spine of a human fetus showing irregularities of segmentation. (Drawn from "Human Embryology and Morphology" by Sir Arthur Keith, page 81, Fig. 74, fifth edition, 1933, by permission of the publishers, William Wood and Company, Baltimore.)

Many other theories have been advanced. Klippel and Feil in 1912 believed the condition due to intrauterine inflammation or trauma. Feil in 1919 expressed belief that a high spina bifida was the original lesion and that pressure and trauma later in fetal life resulted in fusion and malformations. Jaubert de Beaujeu and Bloch<sup>25</sup> believe that hereditary syphilis is a factor. Because nerve lesions are not rare, it has been suggested that the original lesion was in the central nervous system rather than in the skeletal system.

# CLINICAL PICTURE

Little has been added to the clinical description of the case originally reported by Klippel and Feil.<sup>28,29</sup> The head in this patient appeared to be resting on the trunk, the thoracic cage rose to the base of the

skull, the hairline was implanted very low, and all movements of the head and neck were greatly restricted. In 1919 Feil<sup>9</sup> outlined the essential characteristics of the syndrome.

Primary characteristics are: (1) Shortness of the neck. The head appears to be directly implanted on the trunk. The neck is broad and the chin approximates and may even rest on the sternum. Occasionally the trapezii stretch winglike from the mastoid processes to the shoulders, suggesting the name of "pterygium colli" or "web neck."
(2) Low implantation of the hairline. (3) Limitation of movements of the head and neck. These movements are painless, the deficiency being purely a mechanical one.

Secondary characteristics are: (1) Scoliosis or kyphoscoliosis. (2) Elevation of the scapulae (Sprengel's deformity). (3) Descent of the nipples of the breast. (4) Torticollis of muscular or osseous origin. (5) Disproportion between the length of the extremities and of the trunk giving the patient an almost simian-like appearance. These are the features of the extreme type. The essential characteristics described above need not all be present. They may occur in whole or in part and with varying degrees of intensity.

Defects have been noted in other parts of the body, frequently congenital in type, such as abnormal dentition, cleft palate, facial asymmetry, deformities of the forearm, clubfoot and clubhand, defects of the trapezii and other muscles, and vertebral deformities in the dorsal, lumbar and/or sacral regions. Disturbances in the nervous system are not infrequent. The following associated findings have been reported: Mental weakness, deaf-mutism, spastic quadriplegia (Guillain and Mollaret;22 Baruch<sup>2</sup>), syringomyelia (Kallius<sup>26</sup>), anesthesias and paresthesias (Roger, Arnaud and Audier<sup>89</sup>), pseudomyopathy (Sicard and Lermoyez), thenar and hypothenar atrophy (Kallius<sup>26</sup>), cervical spasm with difficulty in breathing and swallowing (Bauman<sup>3</sup>), hereditary ataxia of the Marie type or Friedrich's ataxia (Mattirolo and Bertolotti<sup>80</sup>), and mirror movements (Bauman<sup>3</sup>; Willard and Nicholson<sup>44</sup>).

The spinal anomaly is always present at birth although it may not be recognized at the time. If the infant survives, the deformity is compatible with life. Death in adult life is frequently due to an intercurrent acute infection. A familial tendency is noted. Feil reported the syndrome in father and son, Bar<sup>1</sup> in brother and sister, and Kallius<sup>26</sup> in father and daughter, and Sicard and Lermoyez<sup>2</sup> in a mother and three children.

#### PATHOLOGICAL ANATOMY

Feil described specimens which on examination showed (1) a reduction in the number of cervical vertebrae which were fused in whole or in part; (2) the existence of a superior cervical spina bifida; and (3) elevation of the thoracic cage with formation of a cervical thorax which was more or less developed.

Post-mortem specimens reported by Mitchell, 38 Klippel and Feil, 28,29 Feller and Sternberg,17 and others, reveal platyspondyly,5 cervical and fused ribs, congenital elevation of the scapula with or without bony attachment, and deformity of the dorsal, lumbar and sacral segments. In many cases a large triangular opening (spina bifida) is present in the posterior part of the cervical spine and may extend from the cranium to the thoracic cage. The atlas is often fused to the occipital bone and a basilar or craniocervical kyphosis is almost always present. A synostosis between the atlas and odontoid process is a less common finding, while fusion between the second and third cervical segments or of the vertebrae below are more. frequent. Anomalous defects such as a supernumerary lobe of the lung, patent foramen ovale and an interventricular septum have been noted.

# ROENTGENOGRAPHIC FINDINGS

The positions best demonstrating the cervical anomalies on roentgen examination were studied by Feil. He recom.

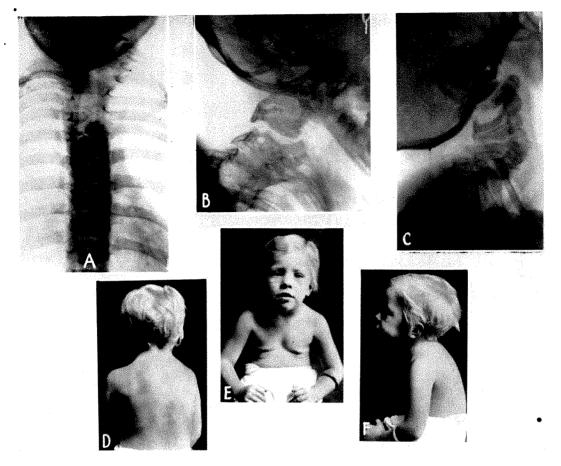


Fig. 2 Case 1. A, shows the ascent of the thorax, bilateral cervical ribs, occult spina bifida of the fifth and sixth thoracic segments. B, shows the fused upper cervical mass separated from the cervicothoracic segments by a distinct hiatus. C, shows a flattening of the cervical curve at its upper portion and acutely angulated forward inferiorly. There are apparently only three cervical spinous processes. The bodies and spinous processes of the cervicothoracic area are fused. Platy-spondyly of the cervical segments is noted. D, E, F, note the short, broad neck, low hair line, round back, the slight tilt of the head to the left and the low nipple line.

mended the right and left oblique anterior, anteroposterior and lateral views. Roent-genograms must be made through the open mouth and by axial projections from the base of the skull in order to secure images of the atlas and axis and their articulations. The findings corroborate and, in the absence of typical clinical manifestations, make the diagnosis.

#### TREATMENT AND PROGNOSIS

There is no therapy for the cervical deformity itself. The condition, if the infant survives, is compatible with life. Massage and stretching may be utilized. Heidecker<sup>23</sup>

reports improvement in mobility after gymnastic exercises. Thomson<sup>43</sup> obtained improvement in a patient by hyperextending the spine on a frame for one-half hour twice a cay. Ryerson<sup>40</sup> divided the outer portions of winged trapezii in one patient with good cosmetic effect. Associated deformities such as scoliosis, torticollis, clubfoot and clubhand should be corrected.

#### CASE REPORTS

Five case reports are herewith presented, including 3 typical cases of Klippel-Feil syndrome and 2 cases of congenital synostosis of the cervical vertebrae. Embryo-

logically the latter may well be interpreted as representing intermediary or interrupted phases of the syndrome, which in the absence of a typical clinical picture might well have remained undiagnosed except for coincidental roentgen findings.

Case 1. J. S., female, aged four, was first examined on May 27, 1935. The family history was negative. The deformity had been noted

fusion of the spine above this area associated with a scoliosis to the left. In the lateral view (Fig. 2C) the cervical spine was flat at its upper portion and acutely angulated forward inferiorly, and associated with an exaggerated dorsal kyphosis. There were apparently only three cervical spinous processes. There was a fusion of the bodies and spinous processes of the lower cervical upper thoracic vertebrae. Platyspondyly of all the cervical segments was

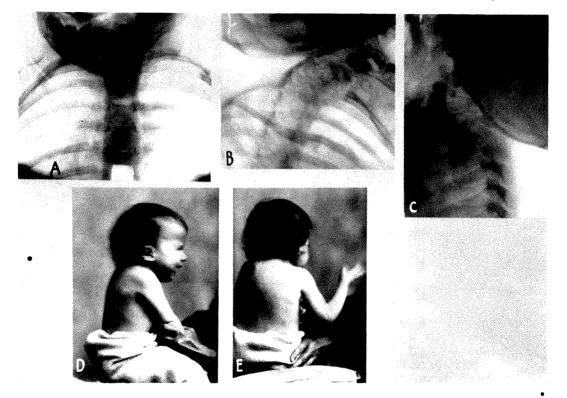


Fig. 3. Case II. A, shows a slight right torticollis; a loss of definition of the upper thoracic spine, platyspondyly and an occult spina bifida. B and C, show irregular segmentation, fusion, and flattening of the vertebral bodies, and an ascent of the thorax. D and E, show the characteristic low hair line, round back and short, broad neck. The head is enlarged and seems to rest on the shoulders.

since birth. She presented a short, broad neck, a low hair line, a round back, and a very slight tilt of the head to the left, with a descent of the nipple line (Fig. 2D, E, F). Dimpling at the lower end of the spine suggested a spina bifida sacralis. A pectus excavatus was noted. The lower extremities were mildly spastic and the patellar reflexes were exaggerated.

Roentgenograms made on June 10, 1935, showed on the anteroposterior view (Fig. 2A) the ascent of the thorax, cervical ribs bilaterally, and an occult spina bifida of the fifth and sixth thoracic segments, with an apparent

noted. The oblique view (Fig. 2B) showed the fused upper cervical mass separated from the lower cervicothoracic segments by a distinct hiatus.

CASE II. M. M., female, aged ten months, was examined on September 23, 1935. The family history was negative. The deformities present had existed since birth. The patient had the characteristic low hair line, round back and short, broad neck of the Klippel-Feil syndrome (Fig. 3D, E). The head seemed to root on the shoulders so that the interval between the mastoid processes and the shoulders was but



one finger-breadth distance. The head was enlarged. She was mentally deficient and unable to sit without support. Associated were bilateral spastic talipes equinus deformities and a double internal strabismus.

Roentgenograms made on October 6, 1936, revealed, on the anteroposterior view (Fig. 3A) a slight right-sided torticollis, a loss of definition of the upper dorsal spine, platy-spondyly and an occult spina bifida. The oblique and lateral views (Fig. 3B and C) showed irregular segmentation, fusion and flattening of the vertebral bodies, with ascent of the thorax towards the base of the skull.

Case III. R. K., male, aged seven (reported through the courtesy of Dr. Harry Subin, Atlantic City). Unfortunately no detailed clinical records of this case were to be had, but from the roentgen examination a rather typical picture may readily be presumed. Roentgenograms made in October, 1936 showed on the lateral view (Fig. 4A) almost complete fusion of the entire cervical spine with shortening of the neck and with platyspondyly especially of the lower segments. An anteroposterior view, not illustrated, evidenced a high spina bifida dorsalis.

CASE IV. B. H., male, aged forty-eight, whose chief complaints were that of chronic low back disability and a left sciatic neuralgia, showed on examination slight limitation of all the movements of the head and neck associated with slight discomfort referred to the cervicothoracic region. No abnormality or deformity could be observed clinically, nor was there a preceding history of injury or infection.

Roentgenograms taken in November, 1936 (Fig. 4B, C) showed incomplete fusion between the second and third, and third and fourth cervical segments and platyspondyly in the lower vertebrae. Additional findings, not illustrated, were spina bifida occulta of the first sacral vertebra, a bifid spinous process of the second lumbar vertebra, and anterior wedging of the upper dorsal segments associated with an exaggerated dorsal kyphosis.

CASE V. E. B., female, aged twenty-nine, was feferred to the senior author by Dr. Jackson Taylor of Coatesville, Pa. She never noted any deformity or discomfort of the neck until September, 19,6, when a falling object struck her on the back of the neck. A painful right torticallis deformity resulted, associated with spasm

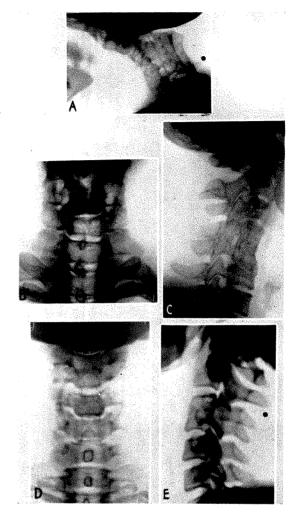


Fig. 4. A, Case III, shows almost complete fusion of the entire cervical spine, a shortening of the neck and platyspondyly. B and C, Case IV, show incomplete fusion between the second and third, and the third and fourth cervical segments and platyspondyly. D and E, Case V, reveal almost complete fusion of the third and fourth cervical vertebrae.

of the cervical muscles, limitation and guarding of the motions of the neck in all directions, actively and passively, and numbness in the right shoulder. She was partially relieved by traction and a Thomas collar. Temporary relief (for one month) followed immobilization in a Calot jacket for a period of three months.

Roentgenographic studies made on November 27, 1936 (Fig. 4D, E) revealed almost complete fusion of the third and fourth cervical vertebrae with no other deformity and without evidence of fracture or disease.

#### SUMMARY

The embryological considerations, the clinical aspects, the the pathological anatomy of the syndrome of congenital synostosis of the cervical spine (Klippel-Feil syndrome) have been described in detail. Three typical cases of the syndrome, two of these with neurological findings, are reported. Two cases of synostosis of the cervical vertebrae are included, as these represent intermediary phases of the cervical maldevelopment. The existence of such congenital anomalies becomes of paramount importance as potential areas of lowered resistance.

#### REFERENCES

- BAR, P. Nouveau-né presentant une singulière malformation de la colonne vertébral (télescopage vertébral). Bull. Soc. d'obst. de Paris, 1903, 6, 425.
- 2. Baruch, R. Kongenitale Halswirbelsynostose (Klippel-Feilsches Syndrom) mit spastischer Teleplegie. Ztschr. f. d. ges. Neurol. u. Psychiat., 1932, 139, 462-476.
- 3. Bauman, G. I. Absence of cervical spine; Klippel-Feil syndrome. J. Am. M. Ass., 1932, 98, 129-132.
- 4. Bertolotti, M. Le anomalie congenite del rachide cervicale. Chir. d. org. di movimento, 1920, 4, 395.
- 5. Buchman, J. Platyspondyly. Arch. Surg., 1937, 34, 23-81.
- 6. CAVE, A. J. E. Two cases of congenital deformity of cervicale vertebrae. J. Anat., 1930, 65, 170.
- CLARKE, J. J. Congenital deformity of cervical spine. Lancet, 1906, 2, 1350.
- 8. Crouzon, O., and Liège, R. Constitution anatomique de la colonne vertébrale dans le syndrome de Klippel-Feil. Bull. et mém. Soc. méd. d. hôp. de Paris, 1928, 52, 917–920.
- Feil, A. L'absence et la diminution des vertèbres cervicales; (étude clinque et pathogénique) le syndrome de la réduction numérique cervicale. Thèse de Paris, 1919.
- Feil, A. Sur la localization du spina bifida dans la région cervicale. Progrès méd., 1920, 35, 510.
- 11. Feil, A. Spina-bifida et anomalies vertébrales. *Progrès méd.*, 1921, 36, 256.
- 12. FeIL, A. Les malformations congénitales du rachis cervical. Vue d'ensemble antomique et clinique. *Progrès méd.*, 1921, 36, 301–307.
- Feil, A. Comment doit-on radiographier la colonne cervicale quand on soupconne l'existence d'une anomalie? J. de radiol. et d'électrol., 1923, 7, 125-133.

- 14. Feil, A. Deux nouveaux cas d'hommes sans cou. Bull. et mém. Soc. anat. de Paris, 1924, . 94, 472-475.
- Feil, A., and Minot. Une nouvelle observation d'homme sans cou. *Progrès méd.*, 1925, 40, 1421.
- Fell, A., Roland, J., and Vanbockstael. Les hommes sans cou; considérations sur la réduction numérique et le tassement des vertébres cervicales. Rev. d'orthop., 1924, 11, 281-304.
- 17. Feller, A., and Sternberg, H. Zur Kenntnis der Fehlbildungen der Wirbelsäule; die anatomischen Grundlagen des Kurzhalses (Klippel-Feilschen Syndroms). Virchow's Arch. f. path. Anat., 1932, 285, 112-139.
- Foggie, W. E. Case of congenital short neck showing Klippel-Feil syndrome. *Edinburgh M.* 7., 1935, 42, 421–428.
- 19. GLADSTONE, R. J., and WAKELEY, C. P. G. Variation of occipito-atlantal joint in relation to metameric structure of cervico-vertebral region. J. Anat., 1925, 59, 195.
- Green, H. L. Unusual case of atlanto-occipital fusion. J. Anat., 1930, 65, 140-144.
- 21. Greig, D. M. Congenital high-scapula. *Edin-burgh M. J.*, 1924, 31, 22-44.
- 22. Guillain, G., and Mollaret, P. Syndrome de Klippel-Feil avec quadriplégie spasmodique. *Rev. neurol.*, 1931, 1, 436–444.
- 23. Heidecker, H. Klippel-Feilsches Krankheitsbild. Beitr. z. klin. Chir., 1928, 144, 303-306.
- 24. Hutchinson. Quoted by Steindler, A. Diseases and Deformicies of the Spine and Thorax. C. V. Mosby Co., St. Louis, 1926.
- 25. JAUBERT DE BEAUJEU, A., and BLOCH, E. Un cas de syndrome de Klippel-Feil. *Acta radiol.*, 1931, 12, 140-145
- Kallius, H. U. Die Missbildungen der Halswirbelsäule, insbesondere über des sogenannten Klippel-Feilsche Syndrom. Arch. f. orthop. u. Unfall-Chir., 1931, 29, 440-466.
- 27. Keith, Arthur. Human Embryology and Morphology. Fifth edition. William Wood & Co., Baltimore, 1933.
- 28. KLIPPEL, and FEIL, A. Anomalie de la colonne vertébrale par absence des vertèbres cervicales; cage thoracique remontant jusqu'à la base du crâne. Bull. et mém. Soc. anat. de Paris, 1912, 87, 185–188.
- 29. KLIPPEL, and FEIL, A. Un cas d'absence des vertèbres cervicales avec cage thoracique remontant jusqu'à la base du crâne (cage thoracique cervicale). N. icong. de la Salpêtrière, 1912, 25, 223–250.
- 30. Mattirolo, G., and Bertolotti. Soria una malformazione rara dell'estremo chalico della colonna vertebrale. Gior. d. r. Accad. di med. di Torino, 1920, 26, 3-12.

31. Meisenbach, R. O. Absence of cervical spine; report of case. Am. J. Orthop. Surg., 1912–1913, 10, 647.

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- 32. MEYER, A. W. Fusion of three cervical vertebrae. *Anat. Rec.*, 1915, 9, 500.
- MITCHELL, H. S. Klippel-Feil syndrome (congenital webbed neck). Arch. Dis. Childhood, 1934, 9, 213-218.
- 34. NAYAK, U. V. Case of abnormal atlas and axis vertebra. J. Anat., 1931, 65, 399-400.
- 35. Noble, T. P., and Frawley, J. M. Klippel-Feil syndrome; numerical reduction of cervical vertebrae. *Ann. Surg.*, 1925, 82, 728-734.
- PAGE, C. M. Case of congenital deformity of dorsal and cervical vertebrae. Proc. Roy. Soc. Med., Lond. (Sect. Orthopaed.), 1923–1924, 17, 34.
- 37. PRITCHARD, E. Case of Klippel-Feil syndrome. Brit. 7. Child. Dis., 1932, 28, 215.

- 38. PRITCHARD, E. Congenital malformations of the neck (Klippel-Feil's disease or web-neck). *Proc. Roy. Soc. Med.*, 1934, 27, 1007.
- 39. Roger, H., Arnaud, M., and Audier, M. Les manifestations nerveuses du syndrome de Klippel-Feil. *Marseille-méd.*, 1934, 1, 233-244.
- 40. Ryerson, E. W. Discussion of paper by Bauman, ref. 3.
- 41. SEVER, J. W. Congenital anatomical defects of spine and ribs. Boston M. & S. J., 1922, 186, 799-821.
- 42. SMITH, G. E. Significance of fusion of atlas to occipital bone, and manifestation of occipital vertebrae. *Brit. M. J.*, 1908, *2*, 594–596.
- 43. Thomson, J. Case of Klippel-Feil syndrome. Arch. Dis. Childhood, 1937, 12, 127-131.
- 44. WILLARD, deF. P., and NICHOLSON, J. T. Klippel-Feil syndrome. Ann. Surg., 1934, 99, 561-567.



# OSTEOPETROSIS ASSOCIATED WITH HODGKIN'S DISEASE

# REVIEW OF THE LITERATURE AND REPORT OF CASE\*

By HARRY HERSCHER, M.D.,† and JUSTIN J. STEIN, M.D. HINES, ILLINOIS

IN 1904 Albers-Schönberg<sup>1</sup> described a rare disease characterized by generalized osteosclerosis, anemia, and enlargement of the liver, spleen and lymph nodes. Because the normal trabecular structure of the bones was obliterated and replaced by a generalized homogeneous density, not unlike marble in appearance, he attached the name "marble bones" to this condition. In 1022 Davis reported the first case in America; and in 1930 Pirie<sup>14</sup> in presenting a series of 3 cases occurring in one family described the development of these interesting bone changes. He discovered that the bones, while exhibiting a marked increase in density, yielded readily to instrumentation and were extremely brittle. From these findings Pirie concluded that the calcium carbonate deposited in the bones resembled chalk rather than marble and he suggested the name "chalky bones." Karsner8a suggested "osteopetrosis" as a name for the condition. It is interesting to note that the brittleness of the bones gives rise to the symptom most commonly associated with the disease, and that it is this symptom, namely multiple fractures, that most often brings the patient to the physician. Since the original presentation by Albers-Schönberg 90 cases have been recorded in the literature of which our case represents the first in which the condition was associated with Hodgkin's disease. Since enlargement of the liver, spleen and lymph nodes occurs almost invariably in Albers-Schönberg's disease, these findings were at first interpreted as a feature of the latter condition. Histological sections, however, revealed the undoubted presence of Hodgkin's disease as well, its authenticity being verified by various competent pathologists. A case of osteopetrosis compli-

cated by osteogenic sarcoma was reported by Kerr<sup>9</sup> in 1936.

#### RELATIONSHIP TO FLUORINE POISONING

In 1936 Spéder, 16 while studying a case of Albers-Schönberg's disease in a Moroccan native, was struck by the resemblance in the bone changes he found in this condition and those he had previously noted in animals suffering from a disease known as "darmous." The latter condition occurs in animals living in phosphate zones where the drinking water besides containing phosphates is known to contain small quantities of fluorides as well. The disease has been produced in experimental animals by including small amounts of fluorides with their diets over a long period of time. Spéder had noted that Moroccan natives living in the phosphate zones frequently suffered from malformation of the mandible, disturbances in dentition, and even osteomyelitis of the jaw, all of which are commonly found in Albers-Schönberg's disease. Accordingly he made roentgenographic studies of the skeleton in 6 such natives who exhibited marked dental disturbances, and in all findings resembling those of Albers-Schönberg's disease were present. Spéder concluded from these observations that the latter condition was caused principally by chronic fluoride poisoning, and was a relatively common rather than a rare disease.16

That chronic ingestion of fluorides will produce generalized osteosclerosis has long been known. In 1891 Brandl and Tappeiner's reported the findings noted in a dog fed 402.9 grams of sodium fluoride over a period of twenty-one months. The dog died accidentally of illuminating gas poisoning and the autopsy, while revealing to change

<sup>\*</sup> From the Tumor Clinic and Research Unit, Veterans' Administration Facility, Hines, Illinois. Published with the permission of the Medical Director, Veterans' Administration, who assumes no responsibility for the opinions expressed by the authors.

in the blood or liver, showed numerous changes in the bones. There was generalized involvement of the skeletal structures. The bones were chalky white in appearance, hard and brittle. Histological studies revealed the bone structure to be intact. The haversian canals, however, were filled with crystals of calcium fluoride. Similar results were reported subsequently by Stanton and Kahn<sup>17</sup> and others.

DeEds<sup>6</sup> demonstrated further that dogs fed on diets containing fluorides showed not only the bone changes noted above but dental defects, anemia and cachexia as well. These symptoms are commonly found in Albers-Schönberg's disease. DeEds expressed the opinion that in humans ingested fluorides were only partially eliminated, a certain portion being fixed as calcium fluoride and deposited in the bones and teeth.

Bishop<sup>2</sup> made careful roentgenological studies of the bone changes in a human being suffering from chronic fluoride poisoning. The bones showed a generalized increased density without alteration of their normal architecture. The increased calcification extended, however, to the ligamentous attachments. The earliest changes were found in the spine and pelvis, following which the bones of the extremities became involved. The margins of the bones became indistinct in outline due to extension of the calcification to adjacent soft tissue structures. Osteophyte formation, calcification of the intervertebral ligaments, roughening of the margins of the pelvis, and extension of bony spicules from the pubes and ischia into the soft tissues were noted. Flemming-Møller and Gudjonsson<sup>7</sup> noted increased calcification of the costal cartilages as well. • Neither the latter authors nor Bishop mention the possibility of an etiological relationship between chronic fluoride poisoning and Albers-Schönberg's disease. 15 The roentgenographic findings in the latter condition resemble those noted in chronic fluoride poisoning in many respects. There is a generalized increase in density affecting the greater portion, if not the entire skele-. ton. The bones first involved are the spine and pelvis; later the proximal ends of the

humeri, the distal ends of the tibiae and fibulae, the base of the skull, and the posterior clinoids are involved. Eventually the remainder of the skeleton may become involved. The trabeculae are partially or completely obliterated. The medullary canal similarly is obliterated, either in part or completely, so that the bones exhibit an amorphous, homogeneous density delimited by their contours. Other findings in this condition include stratification of the bones particularly in the extremities, so that bands of greater and lesser density may be seen running parallel to the epiphyseal lines. This process, while more common at the ends of the bones, may extend into the shafts and may even involve the entire bone. The posterior clinoids frequently show club-like thickening. The ends of the long bones may at times exhibit symmetrical widening. The extension of calcification into ligaments and other adjacent soft tissue structures has not been noted by the authors.

Among the concomitant roentgenological findings are multiple fractures, generally well healed by abundant callous formation, thickening of the periosteum and deformities of the mandibles and maxillae. Not infrequently a superimposed suppurative process is found involving the mandibles, maxillae, or more rarely, the long bones. Rickets is occasionally found as an associated condition. Hydrocephalus, epiphyseal deformities, evidences of physical underdevelopment are among the more common associated findings; while disturbances in dentition are an almost universal manifestation.18 Due to the overgrowth of the cranial bones, the foramina of the skull may become narrowed, resulting in pressure atrophy of the nerves emerging through these foramina. The optic nerve is most frequently involved, resulting in restriction of the visual fields; less commonly, disturbances in hearing result from pressure upon the auditory nerves.

#### PATHOLOGY

The pathological findings are confined chiefly to the bones, liver, spleen and lymph nodes. There is an overgrowth of the cortex and spongiosa of the bone at the expense of blood vessels, fatty and myeloid tissues. The spongiosa may become so dense that it is indistinguishable from the cortex. The medullary canal is encroached upon and may become completely obliterated. The individual trabeculae are thickened and greatly increased in number. By means of polarized light the lamellar structures are found to be distorted and the haversian canals malformed. The liver, spleen and lymph nodes are gen-

#### HISTOLOGY

erally enlarged and fibrotic.

Histological studies reveal an abnormal amount of osteoid tissue in the bones. (Even the medullary cavity may contain large amounts of osteoid tissue.) Osteoblasts are present in abundance throughout the cortex and spongiosa. <sup>8,13,19</sup> In some areas osteoclasts may be seen actively producing lacunar absorption. <sup>4,10</sup> This process, however, is soon replaced by renewed osteoblastic activity with a new laying down of dense irregular trabeculae. <sup>11,19</sup> It is apparent throughout that osteoblastic activity far exceeds osteoclasis and bone formation is in excess of resorption. <sup>19</sup>

The bone marrow is replaced by fibrous tissue in the meshes of which scattered islands of hematogenic elements are noted. Excessive fibrosis is noted in the liver, spleen and lymph nodes and hemopoiesis is depressed.<sup>4,10,11,12,19</sup>

The histogenesis of the abnormal bone structure has been carefully studied by Laubmann<sup>11</sup> and Zwerg and Laubmann.<sup>19</sup> The precartilaginous connective tissue lays down a cartilaginous ground substance. An abundance of cartilaginous cell capsule is noted in which is deposited a relatively large amount of calcium. Primary trabeculae are formed by the numerous, highly activated osteoblasts, but resorption of the primary trabeculae is delayed. Secondary trabeculae cannot thus be formed. There is evidently a disturbance in the endosteal and endochondral metabolism of bone due

to the action of some unknown primary osteoblastic agent. Consequently, bone formation is far in excess of bone resorption.

#### BLOOD FINDINGS

The blood picture presents evidence of the disturbances in hemopoiesis. There is generally a severe anemia of the hypochromic type. In adults the anemia may be mild in degree and even absent. Hyperchromic anemia is occasionally found. The degree of anemia varies considerably but there is no necessary relationship between its severity and the extent of bone involvement.12 It is always marked before death. In the blood smear immature red blood cells (chiefly normoblasts with an occasional megaloblast) are found.12 The platelet count is often low. The leukocyte count is high in children but may be normal in adults. In the terminal stage a blood picture resembling leukemia may develop.

#### PROGNOSIS

The course of the disease varies considerably with the age of the patient. In infants and young children the symptoms are, as a rule, severe. The anemia is generally marked and the prognosis is bad, particularly when hydrocephalus or a leukemic blood picture is found. In adults the disease is more benign in character; indeed it may be in an arrested state. The blood picture may be entirely normal and symptoms may be absent. The tendency to fracture with relatively little trauma brings the patient to the physician and the true nature of the disease, which would otherwise have gone undiscovered, is revealed after a roentgenogram for a supposedly simple fracture shows extensive osteosclerosis of the bone. The disease may exhibit stages in which progression and arrest alternate, accounting, perhaps, for the alternating bands of greater and lesser density sometimes found in the long bones. In the majority of cases the disease is progressive in character and death results either from progressive anemia, intercurrent infection or cachezia resulting from extensive suppurative disease of the bones.

#### TREATMENT

There is no specific therapy for an uncomplicated case of osteopetrosis. The anemia may be treated by the use of various iron and liver preparations available. The general health of the patient should be maintained as well as possible and precautions taken against trauma and secondary infections. Calcium and cod liver oil should not be used.

#### ETIOLOGY

The etiology of osteopetrosis is unknown. There may be a variety of factors responsible for its production. 12 The relatively benign course of the disease in adults as compared to infants and young children suggests the possibility of a different set of operative factors in the former group. The causes of this disease may be similar in some respects to those producing other diseases of the hemopoietic system. Any attempt to arrive at an ultimate cause must of necessity properly evaluate those factors which are most commonly found associated with the condition. Those which are known and which were recognized soon after the first description of the disease are: the familial tendencies; the high incidence in parents and grandparents of patients suffering from the disease; and the predominance of the condition in infants and young children. Albers-Schönberg recognized the familial tendencies. Subsequently other investigators demonstrated this conclusively. McPeak<sup>13</sup> reported 8 cases occurring in three generations of one family. Pirie,14 d'Istria,8 and others, similarly have reported cases occurring in more than one member of the same family. These factors strongly favor the belief that the disease • results from some defect in the primitive germ plasm. Kudrjawtzewa<sup>10</sup> believed the disease was caused by a mutation of the germ plasm, resulting in a dyscrasia of that portion of the mesenchyme which in its evolution is destined to form the hemopoietic system. The high incidence among relatives speaks for a hereditary factor which is carried as a mendelian recessive and is therefore accentuated by inbreeding. The

preponderance of cases occurring in infants and young children gives added weight to the latter contention.

While it must be admitted that generalized osteosclerosis may be produced by a variety of causes, not all cases of osteosclerosis are to be considered Albers-Schönberg's disease. Chronic fluorine poisoning doubtless will produce a generalized osteosclerosis, but the extension of calcification to the soft tissues, ligaments, and other periosseous structures in the latter condition, as described by Bishop,2 Flemming-Møller, and others seems to differentiate this condition from true Albers-Schönberg's disease. Moreover, the presence of calcium fluoride crystals in the haversian canals in the former case with practically no disturbance in the architecture of the bone<sup>6</sup> is at marked variance with the histological picture described in Albers-Schönberg's disease.19 Generalized osteosclerosis has been produced in rats by Selve with concentrated parathormone extracts. Phosphorous poisoning frequently produces bone changes which simulate those in Albers-Schönberg's disease: notably necrosis and osteomyelitis of the mandible, disturbances in dentition, and even stratification of the long bones.

Pirie believed that a generalized epiphystis was responsible for the bone changes found in Albers-Schönberg's disease. The histological picture does not, however, bear out such a contention. Moreover, as Mc-Peak has pointed out, the relative absence of general symptoms in this condition is at variance with what one might expect in so widespread an epiphysitis. Then, too, in the bones of the hands and feet, which have only one epiphysis, the disease may be found simultaneously at both ends. These considerations, along with the concomitant enlargement of the liver, spleen, and lymph nodes, an enlargement which, as Clairmont and Schinz4 and others pointed out, is not a compensatory phenomenon, but rather a developmental defect just as the changes in the bones are, militates against Pirie's contention.

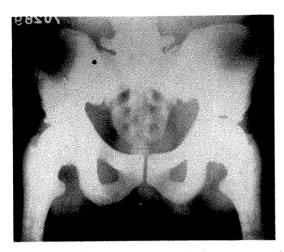


Fig. 1. Film of pelvis showing typical appearance of osteopetrosis.

There appears to be no definite relationship to endocrine disturbance. Pehu and his coworkers found a parathyroid tumor in their case, but this doubtless was a coincidental finding as Hodgkin's disease was in our case. In none of the other cases reported was there any notable endocrine disturbance.

#### CASE REPORT

The patient, A. M. R., a white male, aged forty-one, was admitted to the Edward Hines, Jr. Hospital on May 19, 1937. His chief complaint was pain and swelling in the right ankle associated with large nodes in the right inguinal region.

Family History. Father was born in Iowa, living, aged eighty-six, health good. Mother was born in Missouri, died in 1927, at the age of seventy-one, of heart disease. Two brothers living and well. Two brothers dead, one killed accidentally, and one died of "stomach trouble." Two sisters living and well. Two sisters dead, causes unknown. No history of fractures.

Personal History. Had measles, mumps, whooping cough, and smallpox in childhood. No other illnesses except present one. Fractured his left arm falling off a ladder in 1930. This fall was of sufficient force to produce a fracture in a normal bone. Smokes one package of cigarettees daily; drinks beer and whiskey occasionally but not to excess. Has had no operations. Denies venereal infection. Married and has three children all of whom are in good health. No history of fractures. The patient has lived near Eldon, Missouri, all his life.

Present Illness. Patient states that he was well until May, 1938, at which time he first noticed swelling and pain in his right ankle. At the same time enlarged nodes in both inguinal and axillary regions appeared. Loss of 12 pounds in weight during past year. Also gradual loss of strength. Inventory by systems negative.

Laboratory Examination. Wassermann and Kahn reactions negative. Blood count: red blood cells, 4,030,000; white blood cells, 10,000; hemoglobin, 80 per cent. Differential count: polymorphonuclear leukocytes 68 per cent; lymphocytes 28 per cent; monocytes 4 per cent. Blood chemistry: calcium 12 mg. per 100 cc.; inorganic phosphorus 2.58 mg. per 100 cc. Histological report: Microscopical examination of tissue removed from the left inguinal region reveals a diagnosis of Hodgkin's disease. This was confirmed by several other pathologists.

Radiation Therapy. Patient received a total of 600 roentgens to the right side of the neck;

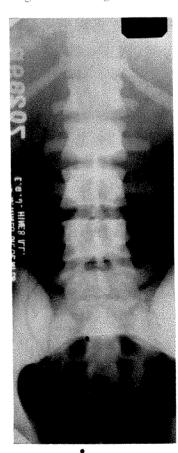


Fig. 2. Anteroposterior film of lumber vertebrae showing them to be dense and with loss of usual detail.

600 r to the left side of the neck; 600 r to the right axilla and also 600 r to the left axilla; 1,000 r to the right groin and 1,000 r to the left groin. Factors of treatment: 200 kv., 0.5 mm. Cu and 2 mm. Al, 50 cm. target-skin distance and 20 ma. The patient improved considerably

remainder of the physical examination is essentially negative.

Roent en Examination. The bones of the skull and face show a slightly uniform increase in density. The sella turcica is normal in size and structure but is denser than normal. There is no

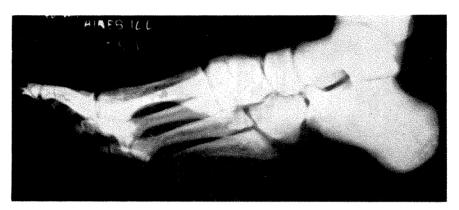


Fig. 3. Lateral film of the foot showing marked increase in density of the bony structures,

and the lymph nodes regressed. He was discharged on July 23, 1937.

He was re-admitted on February 24, 1938, because of loss of strength, enlarged inguinal lymph nodes, and edema of the scrotum, penis, and ankles. Roentgenograms were taken of his entire skeleton and revealed the same changes as on his previous admission. Laboratory findings were essentially the same as before with the exception of urinary findings suggestive of nephritis. Bence-Jones protein was not found in the urine on either admission. Blood calcium and phosphorus were also normal There was a mild secondary anemia on this admission. He received radiation therapy to the right and left groins and was discharged improved on April 13, 1938.

Physical examination reveals an ambulant white male, well developed and neurished, appearing chronically ill. The lymph nodes in the neck, axillae, and groins, are enlarged. The nodes are firm in consistency and not tender on palpation. Both ankles and feet are edematous. There is marked edema of the penis and scrotum secondary to lymphatic obst-uction. The liver and spleen are enlarged. The left elbow is partially ankylosed as a result of an old fracture near the elbow joint. The patient also had an eczematoid dermatitis on admission which is occasionally seen accompanying Hodgkin's disease. The visual fields and eyegrounds are normal. The teeth are in poor condition. The

evidence of intracranial pressure. Roentgen examination of the chest reveals the heart and lung fields to be normal; however, the entire bony framework of the chest has an ivory ap-



Fig. 4. Bones of the wrist and hand are also involved.

pearance. The cervical, thoracic and lumbar vertebrae are quite dense. The bones of the pelvis, sacrum and coccyx are all involved. All long bones show a homogeneous increase in density with loss of detail and obliteration of the medullary spaces. The carpals, metacarpals tarsals, metatarsals, and phalanges all show marked involvement.

#### SUMMARY

- 1. A case of Albers-Schönberg's disease (marble bones) associated with Hodgkin's disease is presented. This is the only case found in the literature.
- 2. The relationship of Albers-Schönberg's disease to fluorine intoxication is discussed. It is the belief of the authors that the type of osteosclerosis produced by such intoxication differs from true Albers-Schönberg's disease in that the excessive calcification in the former condition frequently extends into the adjacent soft tissue structures; such is not the case in the latter disease. Histological studies, furthermore, show well defined differential features in the two conditions.
- 3. While the etiology of Albers-Schönberg's disease is unknown, the high incidence in parents and grandparents of patients suffering from the disease, the greater incidence in infants and young children and the frequent occurrence in more than one member of a family point to a hereditary defect in the germ plasm carried as a mendelian recessive factor and accentuated by imbreeding. This defect apparently results in a disturbance in metabolism which affects the entire hemopoietic system. There is excessive osteoblastic activity involving the greater portion of, if not the entire skeleton; and an associated fibrosis and enlargement of liver, spleen and lymph nodes. Hemopoiesis is generally depressed.

#### REFERENCES

1. Albers-Schönberg, H. E. Röntgenbilder einen seltener Knockenkrankheit. München. med. Wehnschr., 1904, 51, 365.

 BISHOP, P. A. Bone changes in chronic fluorine intoxication. Am. J. ROENTGENOL. & RAD. THERAPY, 1936, 35, 577-585. 3. Brandl, J., and Tappeiner, H. Ueber die Ablagerung der Fluorverbindungen im Organismus nach Fütterung mit Fluornatrium. Ztschr. f. Biol., 1891–1892, 10, 518–539.

4. CLAIRMONT, P., and SCHINZ, H. R. Klinische, röntgenologische und pathologischanatomische Beobachtungen zur Marmorknochenerkrankung. *Arch. f. klin. Chir.*, 1924, 132, 347–380.

 Davis, G. G. Osteosclerosis fragilis generalisata. Arch. Surg., 1922, 5, 449–463.

6. DEEDS, F. Chronic fluorine intoxication; a review. *Medicine*, 1933, 12, 1-60.

 FLEMMING-Møller, P., and Gudjonsson, Sk. V. Massive fluorosis of bones and ligaments. Acta radiol., 1932, 13, 269-294.

 D'Istria, A. Su di un caso di "marmorknochen" malattia di Albers-Schönberg. Radiol. med., 1928, 15, 473-485.

8a. Karshner, R. G. Osteopetrosis. Am. J. Roentgenol. & Rad. Therapy, 1926, 16, 405.

- KERR, H. D. Case of osteopetrosis (marble bones) complicated by osteogenic sarcoma. Am. J. ROENTGENOL. & RAD. THERAPY, 1936, 35, 212-214.
- KUDRJAWTZEWA, N. Ueber Marmorknochenkrankheit. Arch. f. klin. Chir., 1930, 159, 658– 687.
- 11. LAUBMANN, W. Ueber die Knochenstruktur bei Marmorknochenkrankheit. Virchow's Arch. f. path. Anat., 1935, 296, 343-357.

12. McCune, D. J., and Bradley, C. Osteopetrosis (marble bones) in an infant. Am. J. Dis. Child., 1934, 48, 949-1000.

 McPeak, C. N. Osteopetrosis; report of eight cases occurring in three generations of one family. Am. J. Roentgenol. & Rad. Ther-Apy, 1936, 36, 816–829.

14. Pirie, A. H. Development of marble bones. Am. J. Roentgenol. & Rad. Therapy, 1930, 24, 147-153.

- 15. SPÉDER L'ostéopétrose généralisée au "marmorskelett" n'est pas une maladie rare; sa fréquence dans l'intoxication fluorée. J. de radiol. et d'électrol., 1936, 20, 1-11. Abs. Am. J. ROENTGENOL. & RAD. THERAPY, 1937, 38, 506.
- 16. SPÉDER, E., and FOURNIER. Étude radiographique des lésions osseuses du darmous ou fluorose des régions phosphatées du Maroc. J. de radiol. et d'électrol., 1936, 20, 116–122. Abs. Am. J. ROENTGENOL. & RAD. THERAPY, 1937, 38, 508.

STANTON, J. N., and KAHN, M. Sodium fluorid poisoning. J. Am. M. Ass., 1915, 64, 1985.

18. Wortis, H. Osteopetrosis (marble bones). Am. J. Dis. Child., 1936, 52, 1148–1157.

19. Zwerg, H. G., and Laubmann, W. Die Albers-Schönbergsche Marmorkrankheit. Ergebn. d. med. Strahlenforsch., 1936, 7, 95-136.

# STUDIES OF HUMAN NERVOUS AND RELATED TISSUE BY THE ROENTGEN-RAY DIFFRACTION METHOD AND THE PETROGRAPHIC MICROSCOPE\*

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THE problem of applying roentgen-ray diffraction measurements to the study of materials met in biology and medicine is still new and we are somewhat in the position of the early histologists who could make only fundamental observations, as contrasted with the modern pathologists who, in practically every instance, give a complete diagnosis. A number of investigators<sup>1,2,3,4</sup> have begun the study of tissue and the nervous system in lower animals by the use of roentgen-ray diffraction methods. The most recent as well as the most extensive work has been done by Clark and his associates. 4.5,6,7 Up to the present time, however, little work has been done on human nervous tissue.

In this study we are investigating the fine structure of the human brain, and the vagus and sympathetic nerves, together with some of the related structures, such as dura and some tumors.

The experimental diffraction work was done with a Philips Metalix copper target tube. Three and 5 cm. distances were used. All of the patterns reproduced for illustration, however, were taken at 5 cm.

As is well known, this method of investigation can be used to gain direct information about the size, composition, and arrangement of structural elements which lie beyond the range of the ordinary microscope. Much work has been done on the structure of natural fibers such as silk, wool,<sup>9</sup> and cotton.<sup>10</sup> It was found in all instances that the large organic molecules and micelles were arranged or "oriented" so that their long axis was parallel to the length of the fiber, that is oriented along the line of a definite directional stress.

With this in mind, it was hoped that the same method might be applied to the study of nervous and related tissue and in this way we could learn more of their actual submicroscopic structure, thus obtaining a better understanding of the individual characteristics of different types of structure in both their normal and pathological states.

Early in this investigation, it was found

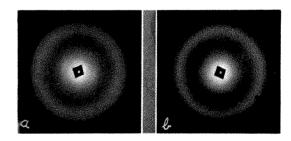


Fig. 1. a, vagus nerve, longitudinal section; b, submaxillary ganglion.

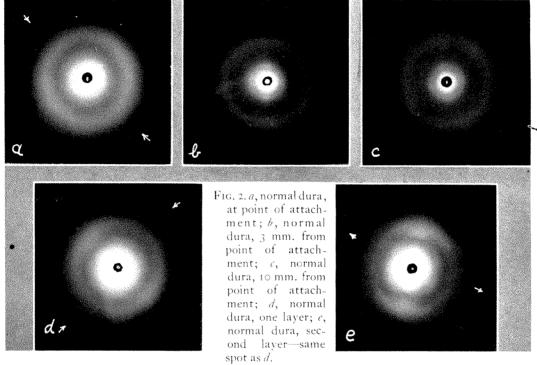
that some types of nerve structures showed a high degree of orientation while others did not.

In diffraction patterns, molecular orientation along a given axis of the sample may be shown by a sharpening and an intensification of the circles of the pattern into arcs, the sharper the arc the greater the degree of orientation. This is illustrated by Figure 1a which is a longitudinal section of the adult vagus nerve. The more sharply defined arcs appear at the longer spacings of 12.3 Å. There is some orientation shown by the faint arc at 2.86 Å. In contrast, Figure 1b is a longitudinal section of the adult human submaxillary ganglion from the same individual and treated in the same manner, but showing no orientation.

<sup>\*</sup> Read at the Thirty-ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 20-23, 1938.

Instead, the spacing, which is divided into arcs in the vagus nerve and corresponds to 12.3 Å., is shown as a continuous ring. In the nerve trunks in general the property of orientation can be noticed in those which have a highly specialized directional function, but, as would be expected, is absent in both the gray and the white matter of the brain and in the ganglia so far investi-

to the origin of meningiomas might be obtained since Cushing and Eisenhardt, 10 as well as other authorities, have shown that there are such definite areas favored for this type of tumor. This analysis is not yet completed, and will necessarily have to continue over a long period of time. Certain results have been established and will be discussed in the following.



gated, in both the sensory-motor and the sympathetic systems. It is possible that certain organized tracts through the brain are oriented, but this has not been shown by our diffraction patterns. Photographs taken in polarized light, as shown later, do, however, show evidence of whole groups or tracts of nerve fibers in the white matter (Fig. 8).

This property of orientation is also well illustrated by the dura. A study was started to map out the surface of the dura along with the underlying tissue in order to determine the degree and direction of orientation with respect to normal points of stress and normal interfering structures. It was hoped that in this manner an index

A narrow strip of whole dura was taken in the parietal region about 3 cm. below the midline, beginning at a point of attachment and extending back for a distance of 2 cm. Figure 2a is the diffraction pattern taken directly on the point of attachment. It shows the beginning of directional orientation, and a general circular arrangement of fibers, such as would be expected in order to maintain good distribution of stress at this point. Figure 2b is taken 3 mm. away from the point and shows a well organized structure with a high degree of orientation. Figure 2c was 10 mm. from the point of attachment and shows a very well defined fiber axis in two directions at 90° to each other. The three patterns show

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that the basic idea being studied, orientation vs. strength required by the tissue to withstand directional stress, is substantially correct. It also emphasizes the necessity of studying the periosteal layer separately from the dura proper. Figures 2d and 2e show precisely the same spot on these two layers, separated and mounted on the diffraction apparatus at exactly the same angle with respect to the beam. It is seen by the fact that the inner arcs of the two layers are approximately 90° to each other that these two layers are each highly

attack such as different methods of drying, some chemical reactions, and the use of various solvents.

The drying experiments were tried first. Diffraction patterns of the fresh undried normal adult brain, either white or gray matter had shown only two diffuse bands,  $\pm 4.64$  and  $\pm 12.0$  Å. The outer band divides into a diffuse band at  $\pm 4.64$  Å, and a broad line at 4.24 Å, upon fixing the tissue in formaldehyde. When the tissue was dehydrated in acetone, these lines sharpened and separated so that more ac-

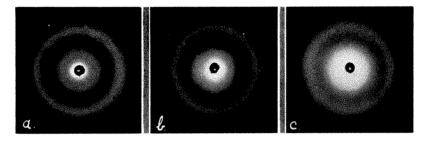


Fig. 3. a, cerebral gray matter dried over CaCl<sub>2</sub>; b, cerebral white matter dried over CaCl<sub>2</sub>; c, meningioma dried over CaCl<sub>2</sub>.

oriented along a fiber axis of their own, and the two axes lie in a plane at an angle of approximately 90° to each other. It is also shown that these two layers have a highly organized structure of their own and that the axes of the two layers of the dura parallel or diverge according to their separate functions and point of attachment. This same arrangement is also shown by the microscopic slides and will be discussed later (Fig. 8). This type of molecular alignment has been shown to exist in other normal biological material such as teeth, bones and white connective tissue—all structures which in their normal function have to withstand directional mechanical stress. In any animal tissue which normally shows orientation, it would seem that the lack of this orientation is definite evidence of some sort of pathology.

Since the untreated cerebral tissue and the pathological material failed to give any very distinct differences, it was thought advisable to try various other methods of curate measurements could be made. A sharp band is then found at 4.18 Å with a somewhat more diffuse band at 4.64 Å, as before. Under these conditions the inner pattern is still too diffuse to allow accurate measurements of long spacings. Acetone drying for a period of one week causes further sharpening of these lines and the appearance of a line about 11.03 Å. Hardening the brain by preserving it in formalin for a long period of time does not give a more complete set of diffraction lines. Under these conditions no difference can be found between the grav and the . white matter of normal brain. If, however, thin sections of brain material are prepared and dried very slowly over calcium chloride or with acetone over a period of twenty days or longer, even clearer and sharper patterns are produced. Under these conditions a difference can be demonstrated between the gray and the white matter of the cerebrum. Figure 3a shows a characteristic pattern of gray matter and

Figure 3b that of white matter. Note that the gray matter shows a less hazy ring in the center at about 9.72 Å—one which has a definite circumference.

Figure 3c shows the pattern from a meningioma which has also been dried over calcium chloride. Note that this pattern has the characteristic protein ring ( $\pm 4.7$  Å) of both the cerebral matter and the dura, but lacks the orientation of the dura,

were run with organic solvents, and the parts extracted by these solvents analyzed separately.

The solvents used were suggested by the work as reported by Bodansky, 11 Schmitt, Bear and Clark, 4 and Page. 12 Of the various solvents used, extractions made with acetone followed by a mixture of 5 per cent alcohol and 95 per cent benzene proved to be the most useful. The following com-

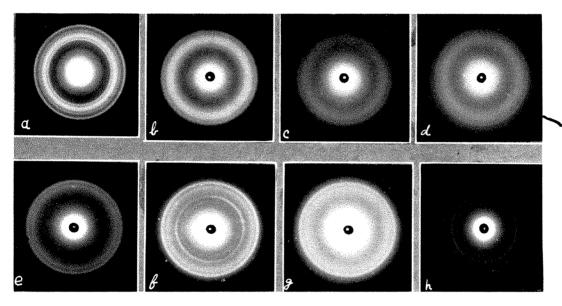


Fig. 4. a, acetone extract from normal cerebral tissue; b, acetone extract from normal dura; c, acetone extract from a chromophobe adenoma; d, acetone extract from a meningioma; e, benzene-alcohol extract from normal cerebral tissue; f, benzene-alcohol extract from normal dura; g, benzene-alcohol extract from a chromophobe adenoma; h, benzene-alcohol extract from a meningioma.

and the 4.2 spacing of the brain tissue is very weak. Table 1 gives all spacings for these dried tissues as well as those for the nerves and dura which have been referred to previously.

Following the drying experiments addition reactions were used. Various metallic salts, acids and bases were used but they have all been generally unsuccessful. Mild bases are the only chemicals so far tried that offer any encouragement.

In the presence of such complex mixtures as brain or tumor substance, one naturally tries to arrive at a differentiation by appropriate chemical or physical separation of components. In this case serial extractions

ments will be concerned with the tissue after extraction and the solutions from the acetone or the benzene-alcohol mixture. All of the tissues used had been preserved for several weeks in formalin. The specimens were cut into thin slices and extracted in a modified Soxhlet apparatus for a • period of twenty-four hours with acetone. The acetone was then replaced by the benzene-alcohol mixture and extraction continued for another twenty-four hours. The solutions were then evaporated, keeping the temperature always below 90°. The sticky residues were then mounted in small loops of nickel wire and the diffraction patterns taken. Figure 4 shows patterns



TABLE I

· Vagus Nerve	Sub- maxillary Ganglion .	Normal Dura	Normal Cerebrum	Normal Cerebrum in Formalin	20 day	rebrum Dried ys over Chloride	Menin- gioma
2.86		2.81			Gray	White	
4.2		4.08		4.24	4.2	4.2	4.1 f
4.64w	4.7 <b>w</b>	4.58 <b>w</b> 6.54	4.64w	4.64w	4.7 W	4.76w	4.76w
12.3	12.3	11.22	12.0W	12,0W	9.72 <b>w</b>	haze	
	3			, 2.0	15.78f	15.36f	

All spacings given in Å

=intense line

w = wide, fuzzy band
f = very faint line

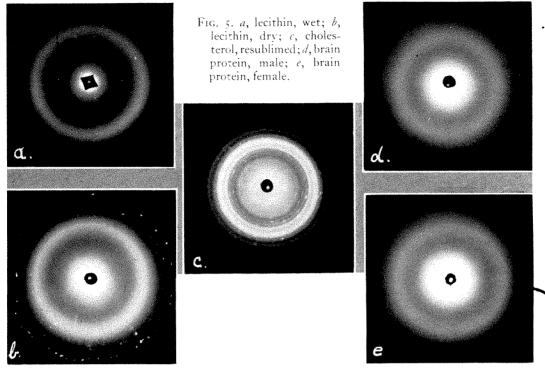
m = light line f = very faint line

of the evaporated extracts—Figures 4a, b, c, and d are the acetone extracts from the normal cerebral tissue, normal dura, chromophobe adenoma tissue and a meningioma, respectively. Figures 4e, f, g, and h are the extracts of the same tissues using benzene-alcohol following the acetone.

Table II gives the complete list of measurements for all of these patterns. It will be noted that there are more lines on the pattern for the adenoma than there are spacings reported. The lines for which there are no spacings given are those from sodium chloride which was in the preserv-

TABLE II

			EXTR	ACTS	_		•
Menin- gioma	Aceto Normal Cerebrum	one Normal Dura 2.8 m	Adenoma	Menin- gioma	Benzene- Normal Cerebrum	Alcohol Normal Dura	Adenoma
3.74f 4.10	3.48wm 3.82m 4.14	3.78f 4.08	4.16	4.12	4.09	3.36m	4.16
• 4.89w	4.5° 4.98 5.14	4.84w	4 · 77 <b>w</b>	4.46	4 · 59W	4.52m	4.56w
,	5.85			5.31m 5.55		5.63	•
	6.3 m 6.88m 8.58m 13.5			6.28m 6.74 12.70f		6.84	
= in <b>t</b> er	17.05 ngs given in Å. nse line , fuzzy band	14.72					•



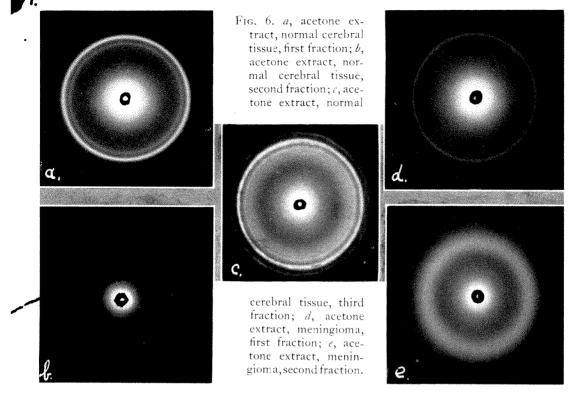
ing fluid. By comparison of these patterns, it can be noted that each specimen gives a pattern or set of patterns which are characteristic of that tissue. The following summary illustrates this point in outline form:

Type of	Acetone	Benzene-Alcohol
Tissue	Extract	Extract
Cerebrum	Complex pattern	Simple pattern
Dura (note	Simple pattern	Complex pattern
inner ring)		
Adenoma	Both extracts giv	e similar patterns
Meningioma	Simple pattern	Complex pattern

The small pieces of material left after extraction were mounted in collodion and examined by the diffraction method. The patterns for these residues are not given separately for they show nothing more than has already been pointed out in whole tissue diagrams. It may be noted, however, that not only these residues and the evaporated extracts, but also the dried tissue to some extent, indicate the presence of a submicroscopic structure in the meningioma, which partakes of the character of both the normal brain tissue and the normal dural tissue.

Since the chemistry of the brain is extremely complicated12 and as yet very incompletely worked out, it is not possible for us to go far at the present time in identifying the chemical entities responsible for these patterns. Rather the purpose of this research was to find basic information characterizing the various intracranial tumors and nerve structures. Nevertheless, of the pure substances known to be present in the brain, all that could be obtained were investigated. Figure 5 shows lecithin in both its forms, a wet and b dry. The presence of this substance makes it necessary to proceed with extreme caution, as its pattern varies widely through a whole range of forms depending upon its moisture content. Figure 5c is the pattern of resublimed cholesterol. Figures 5d and se are the patterns from male d, and female e brain proteins. These samples were very kindly supplied to us by Professor Block.13 With these patterns as standards, we can compare various tissue patterns such as \_\_\_ those of the untreated and treated nervous tissues as well as the patterns from the extracts and determine, at least in part,





the components of these original samples. For this purpose of identification, a more complete extraction was run of the meningioma and the normal cerebral material by first grinding it with well washed sand and then extracting in the Soxhlet apparatus for forty-eight hours with acetone. These solutions were fractionally crystallized. There were three easily distinguishable fractions from the normal cerebral extract but only two from the meningioma. Figure 6 a, b, and c gives the patterns for the three normal cerebral fractions while d and e are the two fractions from the meningioma. Table III gives the spacings for all of these fractions. It will be noted • that the second fraction of the normal is mainly cholesterol and the third fraction probably has some lecithin. The meningioma also seems to show some of spacings characteristic of lecithin -14.7 Å, but the percentage is very low as shown by the faintness of the line. By far the largest amount of the second fraction of the meningiona extract would seem to be of a protein material (see Figs. 5d and e). We

wish to mention that when this acetone extraction of forty-eight hours' duration was followed by the usual alcohol-benzene mixture, no residue was left on evaporation of the latter solvent. The explanation offered for this difference between the twenty-four and forty-eight hour extractions is that a clean separation cannot be accomplished by fractional extraction. Hence by running for a longer period of time several components were taken out which were later separated by fractional crystallization whereas the separating was done mainly by regulating the time of

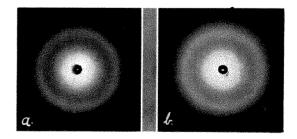


Fig. 7. a, cerebral gray matter extracted with acetone; b. cerebral white matter extracted with acetone.

extraction with the solvent under the first conditions.

The two patterns (Figs. 7a and 7b) of gray and white tissue left after extraction with acetone as well as those (Figs. 3a and 3b) which were dried indicate that there is more than just the protein present since there is a sharpening of the inner ring in the pattern. This along with other indi-

or other biological material which either has optical activity, or in which it can be induced. We will not go into a detailed history of this work, which was started many years ago, since this phase of the subject has been well covered by Schmitt and Bear. 16

A standard petrographic microscope was used for this work rather than the simple

TABLE III
FRACTIONAL CRYSTALLIZATION OF ACETONE EXTRACTS

		Cerebru	m	$\mathbf{M}$	eningio	ma	Lec	ithin	Choles- terol
Total extract	Fractions		Total extract	Fractions		Wet	Dried over CaCl <sub>2</sub>	Crys- talline	
			2.23m 2.48m					2.24	
3.48wf		3 · 44 f	3.14m				3.16f	3.12 3.46	2.97 3.18f 3.5 w
3.82m 4.14	4.12	3.75f 4.12	3·74 4·13	3.74t 4.10	4.15				3.80 4.2
4.5° 4.98	4.58	4.58 4.92	4.6	4.89w	4.58	4.92w	4.64w	4.66w	4.59
5.14		5.20							5.06w
5.85w		5.76w							5.28f 5.94
6.3 m 6.88f		6.20m 6.96m							6.30m 6.98m
8.58m 13.50		8.4 m 13.58				14.7m	13.2m	13.1	8.46m 13.58
17.05		17.05f				. 9			17.05

The purified, extracted protein gave only the diffuse band at 4.76Å.

cated changes lends encouragement to continue the search for a satisfactory method of differentiating the various classes and sub-classes of tumors.

Several workers, most recently Schmitt,<sup>14</sup> and others,<sup>15</sup> have supplemented the diffraction work with observations in polarized light. The ordinary polarizing microscope (chemical microscope) or better, the petrographic microscope is adaptable to the study of biological material such as myelin sheath which is known to be birefringent

polarizing microscope for it was found that with the material used in this study a great amount of detail could be brought out by the use of the selenite plate. This accessory was discovered about 1813 by Biot, and its use together with the physical basis of its action is fully described in the sandard textbooks.<sup>17</sup> By giving a contrast of bright colors the plate makes possible the discovery and determination of very slight double refraction, and the study of very tiny fragments of optically active material.

All spacings given in Å

\_\_=intense line

w = wide, fuzzy band

m = light line

f = very faint line

The introduction of the plate between the crossed nicols causes the field to change (with the stage empty) from darkness to a color which is variously described as "first order red," "sensitive red," "sensitive violet" or simply Biot's original designation "teinte sensible." To us the color is redviolet and the designation "first order red," which is now more or less standard terminology, is used throughout. The color is accurately reproduced in the unoccupied portion of the field in Figure 8a. This accessory plate has been of great value to the crystallographer ever since its discovery. In the present investigation crystals which are too tiny for accurate study without the accessory, or which may be largely concealed in inactive material, become clearly visible, and material which is only slightly birefringent takes on the color of the field only when it is at an angle of extinction. In biological material both situations are frequently met in the same specimen.

So far in this study frozen sections have been used entirely, except in special cases where it is better to "tease out" a few fibers, using needles for the coarse work and finally glass hairs. Where sections are studied these are cut as thin as possible by the frozen section method, preferably from fresh tissue, but very little, if any, difference has been demonstrated as yet between fresh tissue and specimens preserved in formalin and saline for a reasonable length of time. To prevent distortion the sections are handled in saline solution in a Petri dish. They are then mounted and covered in the usual manner with a No. I cover slip and examined at once. Ordi-, narily the saline solution makes no difference in the observation, but if the specimen is to be kept for more than an hour or so it is rinsed through several changes of distilled water to prevent possible precipitation of salt cry tals as the water escapes. With the specimens of nervous and fibrous tissue so far examined we have not been able to demonstrate that either the freezing or the washing with distilled water caused any

disruption of distortion of the structures which become visible in polarized light, although we have investigated this source of error. Specimens which have been heated, or mounted in paraffin or celloidin are entirely unsuitable for study, as are stained specemens in general. The work has been carried on with the close cooperation of Dr. P. F. Morse and the Department of Pathology, and it has been found practical to have both types of investigation made on the same microscopic field by studying the section under the petrographic microscope first and then having the section stained for regular pathological examination. In some cases the gross specimen was divided and one portion mounted in paraffin.

All of the colors shown in the photomicrographs are as seen in the unstained tissue. As might be expected, examination of this untreated tissue by ordinary light does not reveal much detail. With the nicols crossed, myelin and the oriented fibers of the dura stand out sharply and appear brightly lighted in the dark feld. If now the selenite plate is introduced, all of these optically active elements show a great deal more detail. Inactive material and fibers having their fiber axes parallel to the optic axis of the system assume the color of the field, as do also those optically active elements which are exactly at an extinction angle. Birefringent material having an axis perpendicular to the axis of the system, and not at an extinction angle, appears in a brightly contrasting bluegreen or orange-yellow color. As the stage is rotated these interference colors interchange with each 90 degrees of rotation, with the particle being studied disappearing into the background color exactly as its extinct on angle is passing, only to reappear in the next quadrant in the opposite color.

It has been found easy and practical to record the image of the field seen in the microscope by means of color film and a very simple camera. The camera was made from a "Bantam" f 6.3 by removing the lens and fitting an adapter tube, turned out

of an aluminum bar, to the face plate. The adapter tube should fit smoothly over the ocular of the microscope, should permit free rotation without looseness, and must be accurately aligned with the optical axis and perpendicular to the focal plane. Any inexpensive miniature camera may be used, but care should be taken to see that the one chosen has a "time" stop on the shutter. One other accessory is needed for accurate focusing. This is made from a piece of tubing, in this case red fiber, which will fit over the ocular end in the same position as the camera. This tube is slotted at the exact level of the focal plane above the ocular lens and a piece of ground glass inserted and held with adhesive tape. It helps, but is not necessary, to fasten a simple magnifying lens in position above the ground glass and focused upon it. A record photograph is made by focusing the image sharply on this ground glass and interchanging the camera with the focusing tube. More elaborate systems including cameras with lens systems to eliminate the ground glass focusing have been tried and found much less satisfactory.

For the use of color film the exposure must be very accurately determined. We have found the most satisfactory procedure to be the preparation of a strip of test exposures on Eastman Portrait Panchromatic film. The correct exposure time for this film is then multiplied by three for Kodachrome A or by twelve for Dufaycolor. Dufaycolor has an advantage in that it can be processed at once in the laboratory. Kodachrome has other advantages. Examples of both are given.

Figure 8 illustrates the general type of observations which can be made by this method. In addition, exact measurements of refractive index, extinction angles and other crystallographic data can be obtained on very tiny fibers, cell membranes, etc. However, the data of this nature so far obtained must be reserved for later publication.

Sections a, b, and c of Figure 8 show the appearance of a piece of normal dura on the

stage of the petrographic microscope. In section a two layers of oriented fibers are shown in their original arrangement, crossing each other at an angle of 76°. Sections b and c show the same field on a single fiber layer and illustrate the color change and the appearance of fiber detail when the stage is moved through an angle of 45°. (May we note in passing that these reproductions are in actual size, and the magnification given is actual magnification. In use these color slides are usually projected onto a 14×17 inch screen for study. In this way a further "empty magnification" of about 13 diameters is gained, which makes the slide much easier to observe, and is in fact the usual procedure with photomicrographic reproductions.)

Sections d and e are a single fiber from  $\square$ an adult human vagus nerve. The interference colors are illustrated, and in the original a considerable amount of fine detail of the axis cylinder and the myelin sheath are visible. Sections f, g and h are selected from a series of fields. The original specimen consisted of a small piece of dura to which was attached a meningioma about 2 cm. in diameter. The attachment was about 3 mm. in diameter, and the dura was thickened to approximately five times normal around this stem. A suitable slice was cut from the middle of the entire specimen and sectioned. The sections were then examined with the petrographic microscope, a series of fields being taken from the outermost layer of the dura, through the attachment and through the tumor. The field shown in f is similar to normal dura but not quite typical; g shows an intermediate structure with elements similar to the other two, and h is definitely a characteristic structure of a meningioma. The series is offered to illustrate the structural transition from fairly normal fura to meningioma. The field shown in F gure 8i is one of particular interest to us as this small specimen was presented to is as an "unknown" with the hint that "it might be a Cushing's basophile adenoma." Before the petrographic microscope was available

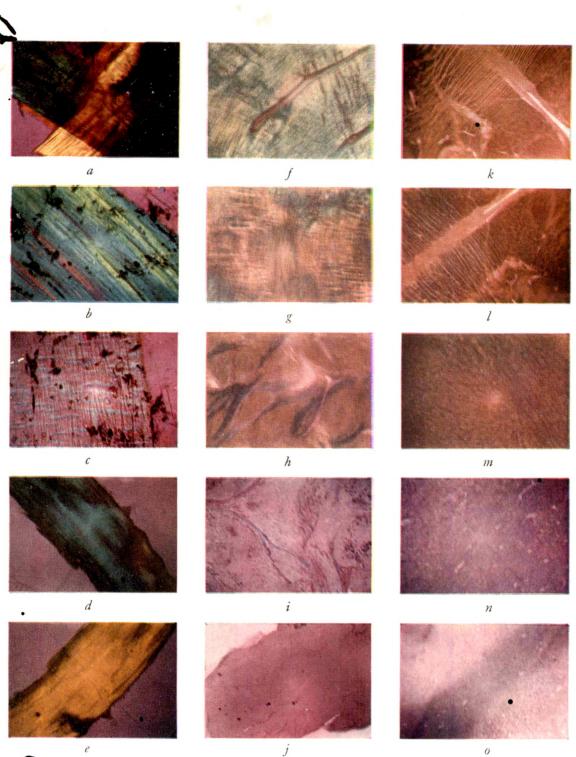


Fig. 8. a, normal dura. Two fiber layers in their original arrangement at 76°. Kodachrome ×100; b, normal dura, single fiber layer. Kodachrome ×100; c, same as b, but the stage has been rotated 45°. Note color change and detail of fibers; d, normal human vagus nerve, single fiber. Dufay ×450; e, same as d but rotate 90°; f, atypical dura at the point of attachment of a small meningioma. Dufay ×100; g, intermediate field between f and h. Note shortness and random curvature of individual fibers, and color variations. Dufay ×100; h, typical field of a meningioma. Dufay ×100; i, suprasellar meningioma. Kodachrome ×100; j, chromophobe adenoma. Kodachrome ×45; k, normal brain stem. Dufay ×45; l, same as k rotated 90°; m, same section as k and l, showing single nerve cell in olivary nucleus. Dufay ×970; n, normal cerebral gray matter. Kodachrome ×100; o, normal cerebral white matter. Kodachrome ×100. (Origin of the specimens is acknowledged in the text. All pathological diagnoses by P. F. Morse, M.D.)

both the extractions and the diffraction patterns had shown the specimen to be a meningioma. The microscope definitely placed it in this class as is shown in the color photograph. The section and the remainder of the specimen were submitted for regular pathological examination and the diagnosis "suprasellar meningioma" was received.

Figure 8j is a portion of a proved chromophobe adenoma, and the section shown includes a small portion of the pituitary stalk. Glandular tissue in general gives no interference colors whatever, but it is to be noted that this section shows a tract of bright green points, characteristic of the appearance of nerve fibers. While this evidence is in no way conclusive it is thought that this type of investigation may throw additional light on the debatable question of the existence of nerve fibers in the pituitary stalk. Figure 8k is taken through the normal brain stem at a level near the rostral end of the olive. A full and detailed description of the structures found at this level is given in Ranson.<sup>19</sup> In this section and the one following the structures which are at once visible are the median raphe, a portion of the inferior olive, medial lemniscus and a large number of tracts and other structural details. Figure 8l is the same field rotated to bring out detail in contrasting color. Section 8m is the same slide as k and l shown under high power. In the upper left quadrant near the intersection of the cross hairs a large single nerve cell of the olivary nucleus is shown. It can be seen that the nucleus, nucleolus, Nissl flakes, chromatin granules and the cell membranes are brought out very clearly by this method.

Figures 8n and o are normal cerebral tissue taken at random; n is normal gray matter showing on an inactive background a large number of small bright green points where single myelinated fibers have been cut through perpendicular to their axis. These transverse sections are of interest because the entire nerve sheath does not show the same interference color in a given

position of the stage. Instead, as the stage is rotated or the focus changed, the spot of interference color is seen to spiral around and up or down the axis cylinder. This indicates that in addition to the types of orientation already studied there is evidently some part of the nerve sheath which has an orientation with a spiral axis of symmetry, which has not yet been investigated. Figure 80 is normal cerebral white matter, showing an oriented tract in an inactive background.

This research in no way invades the field of pathology, nor is it intended ever to do so. Rather it is our purpose to investigate by physical means the wide and comparatively unexplored borderland of the ultimate nature of living tissues, of the large molecules and micelles which make up the structures seen in the microscope and upon which so much excellent work is being done at the present time by the ultracentrifuge and by chemical means. In this paper we have tried to give a general survey of the field of study uncovered by correlating the methods of procedure we have described. In subsequent publications we expect to be able to give more conclusive data on a few of the definite points we have mentioned.

# SUMMARY

- 1. Orientation can be noted, in general, in nerve trunks which have a highly specialized directional function.
- 2. Gray and white matter of the cerebrum give slightly different roentgen-ray diffraction patterns, the difference being shown clearly after drying.
- 3. Extracted brain tissue gives a pattern very similar to that of neuroproteins.
- 4. Extracts of some types of meningiomas show characteristics of both normal brain and of dural tissue.
- 5. Dural tissue is oriented, the degree of orientation varying with the part of the dura being considered.
- 6. The dura proper and the periosteal layer each have their own well defined

orientation which may be parallel or at angles varying up to 90 degrees.\*

To Drs. P. F. Morse and Frederic Schreiber whose help and interest were a great influence in starting and sustaining this research, to Prof. A. J. Derbyshire, Jr., who supplied material, information on neuroanatomy and who with Mr. Robert Emerick assisted us with the actual work, to Dr. Gabriel Steiner who supplied us with material and graciously offered the facilities of his laboratory to cut large numbers of frozen sections, to Dr. Russell H. Morgan who supplied material, and to our large number of friends who have assisted us continuously over a period of more than two years, we extend our grateful thanks.

#### REFERENCES

- 1. Boehm, G. Das Röntgendiagramm der Nerven. Kolloid-Ztschr., 1933, 62, 22-26.
- 2. Handovsky, H. Röntgenographische Untersuchungen an erregter und gelahmter Nervensubstanz. Kolloid-Zischr., 1933, 62, 21-22.
- 3. Herzog, R. O., and Janke, W. Verwendung von Röntgenstrahlen zur Untersuchung metamikroskopischer biologischer Struckturen. Festschr. d. Kaiser Wilhelm Ges., 1921, p. 118– 120.
- SCHMITT, F. O., BEAR, R. S., and CLARK, G. L. X-ray diffraction studies on nerve. *Radiology*,

   1935, 25, 131-151.
- CLARK, G. L. Analysis by x-rays of ultimate structures of living materials. *Radiology*, 1938, 30, 180-190.
- CLARK, G. L., and SCHAAD, J. A. X-ray diffraction studies of tendon and intestinal wall collagen. *Radiology*, 1936, 27, 339-356.
- CLARK, G. L., and SHENK, J. H. X-ray diffraction studies of globular proteins; action of formaldehyde on proteins. *Radiology*, 1937, 28, 357-361.
- \* The use of the methods here suggested has been extended to the study of the brains of experimental animals exposed to various dosages of roentgen radiation. A full report of these experiments is now being prepared for publication.

- 8. CLARK, G. L. Applied X-Rays. Second edition. McGraw-Hill Book Co., Inc., New York City, 1932, pp. 444-447; 451-456.
- 9. FARR, W. K., and Sisson, W. A. X-ray diffraction patterns of cellulose particles and interpretations of cellulose diffraction data. Contrib. Bovce Thompson Inst., 1934, 6, 315-321.
- 10. Cushing, Harvey, and Eisenhardt, Louise. Meningiomas. Charles C Thomas, Springfield, Ill., 1938, Chap. 8.
- 11. Bodansky, M. Introduction to Physiological Chemistry. Second edition. John Wiley & Sons, Inc., New York, 1930, Chap. 3; p. 496.
- 12. PAGE, I. H. Chemistry of the Brain. Charles C Thomas, Springfield, Ill., 1937, p. 54.
- 13. Block, R. J. Chemical studies on the neuroproteins. 1. Amino acid composition of various mammalian brain proteins. 7. Biol. Chem., 1937, 119, 765-768. 11. Effect of age on amino acid composition of human and mammalian brain proteins. J. Biol. Chem., 1937, 120, 467-470.
- 14. Schmitt, F. O. Nerve ultrastructure as revealed by x-ray diffraction and polarized light studies. *Cold Spring Harbor Symposia on* Quantitative Biology, 1936, 4, 7-12.
- 15. SETTERFIELD, H. E., and WEAVER, H. M. Some cytological observations on peripheral myelinated nerve fibers as observed by the polarized light method. *Ohio J. Sc.*, 1937, 37, 65-74.
- 16. Schmitt, F. O., and Bear, R. S. Ultrastructure of nerve axon sheath. *Biol. Rev. Cambridge Phil. Soc.*, 1939, 14, 27-50.
- 17. Johannsen, A. Manual of Petrographic Methods. McGraw-Hill Book Co., Inc., New York, 1918, art. 294, p. 365 et seq.
- 18. Biot, J. B. Mémoire sur un nouveaux genre d'oscillation que les molécules de la lumière éprouvent en traversant certains cristaux. Lu à l'Institute, 3 Nov., 1813; Mém. Acad. France, 1912, XIII; 1814, 1-371.
- RANSON, S. W. Anatomy of the Nervous System, W. B. Saunders Co., Philadelphia, 1934, Pt 374.



# SOME EFFECTS OF ROENTGEN RAYS ON SACCHAROMYCES CEREVISIAE\*

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ALTHOUGH yeast is one of the easiest laboratory test objects with which to work, only a few radiobiological experiments have been carried out with it and, so far as we know, only Holweck and Lacassagne<sup>2,3,4,6,7</sup> and Wyckoff and Luyet<sup>15</sup> have used it for critical quantitative work.†

While these two pairs of investigators used different species of organisms and somewhat different radiations, their results were generally similar. Holweck and Lacassagne used Saccharomyces ellipsoideus and exposed them to ultraviolet (2,800-3,000 Å), soft roentgen rays (8.32 and 1.93 A) and alpha particles, while Wyckoff and Luyet used Saccharomyces cerevisiae and exposed them to ultraviolet (2,536, 2,652, 2,900 and 3,132 Å) soft roentgen rays (1.537 Å) and cathode rays from a Coolidge type cathode-ray tube. Both used quiescent organisms (i.e. from old cultures) and spread them on the surface of agar medium for treatment and culture. The effects observed in both cases were immediate and delayed killing as made evident by differential staining and relative numbers of cells per colony.

The two pieces of work are in agreement in indicating the following: (1) that some cells may be killed outright by the radiations; (2) that others may be injured without being killed; (3) that "S" or skew type (multiple-hit-to-kill) curves are obtained; and (4) that differential quantitative effects are produced by the different qualities of radiation. Both teams of investigators, however, have mentioned that the shifting character of the experimental data tends to cast some doubt on the significance of the

† See references 1, 5, 8, 9, 13 for other qualitative radiobiological experiments with yeasts.

findings. Nevertheless, much has been made of the results in developing the so-called "hit-keory" of the biological effects of radiation.

The present work was undertaken not so much to improve the methods used previously as to try other procedures which might allow more critical analyses. As will be seen, some important variations were obtained. Since the significance of quantitative work may be judged in part by the experimental procedures and conditions used, considerable detail will be given.

#### PART I

The yeast technique first employed was developed by Richards<sup>9,10</sup> who has written extensively on the growth properties of this organism and who spent a week in this laboratory carrying out the first irradiation experiments. We take pleasure in expressing our appreciation and indebtedness to Dr. Richards for his interest, cooperation and kind assistance.

#### Procedure

The procedure used was to expose actively growing cultures of the organisms to varying amounts of radiation and to determine the relative population densities at varying times following irradiation. For this it was necessary to make numerous determinations and do so in a way that would not disturb the growth activities of the cultures. This was made possible by using a phoso-cell instrument developed previously by Richards and Jahn. 12

Yeast, as do many unicellular organisms, manifests a rate of growth which is exponential with time when the growing conditions are optimum. As waste products accumulate and nutritive materials decrease, the rate drops off. The experiments to be described here were carried out in such a way that treatment was ad-

<sup>\*</sup> Acknowledgment is made to the United States Works Progress Administration of New York City for assistance rendered under Project Number 125.

ministered early in the logarithmic phase of growth and determinations of the relative number of organisms present were made during the remainder of this phase and during part of the phase of decreasing growth rate. While we actually measured population densities at various times and thus the rate of growth, the data can be used in a unique way to indicate the relative number of organisms killed by the radiation and how this varies as a function of dose.

The yeast used was a strain of Saccharomyces cerevisiae obtained originally by Richards a few years ago from a single cell isolation. It has been maintained at 26°C. on either liquid or solid media. The liquid medium (Williams14 and Richards<sup>10</sup>) consisted of 20 grams of table sugar (sucrose), 3 grams of ammonium sulphate, 2 grams of potassium di-hydrogen phosphate, 1.5 grams asparagin, 0.25 gram of calcium chloride, 0.25 gram of magnesium sulphate in I liter of distilled water. For solid media 23 grams of Bacto-Nutrient Agar was added to the above. To obtain material for the experiments, organisms were transferred from an agar slant to liquid medium. This was done by placing a straight platinum wire in the center of the slant colony, moving it back and forth over a space of about 1/8 inch and transferring at once to a tube containing 13 cc. of liquid medium where the wire was washed free of the inoculum by moving through the medium. The inoculated material was then allowed to incubate for three days after which 3 cc. of uniform suspension was diluted with 27 cc. of fresh liquid medium. Thus I cc. of this culture represents o.1 cc. of three day old culture. This was the material used for experimentation and will be referred to simply as the test material.

One cubic centimeter of test material was transferred by means of sterile pipettes to each of twelve celluloid containers. These were circular, 2.46 cm. in diameter, 1.2 cm. deep and fitted with covers. The thickness of the celluloid of the containers and the covers was 0.3 mm. Two containers with media were placed in a sterile petri dish and kept as controls. The other ten were placed on a thin (0.1 mm.) celluloid tray and arranged under the roentgen tube for exposure. The reason for using celluloid in these two places was to avoid as much as possible complications arising from scattered radiation.

#### Treatment

Exposures were carried out using a roentgen

machine under the following conditions: 200 kv., 30 ma., 33.6 cm. distance and no filter except the heavy glass of the roentgen tube (0.6 cm.). The intensity of the radiation at the point of treatment (measured in air) was 291 roentgens per minute. The output was kept constant during treatment by means of a galvanometer which was attached to an ionization chamber that remained in a fixed position in a part of the roentgen-ray beam not being used for treatment purposes. Two celluloid containers were removed after receiving each of the following exposures: 0, 8, 16, 32, 64, and 128 minutes.

After treatment the irradiated material together with the non-irradiated controls were transferred to culture tubes (Pyrex test tubes 1.5 cm. in diameter and 15 cm. in length) and further diluted with liquid medium. This was done with a sterile pipette and rubber bulb, one for each individual sample. The test material was drawn up from the celluloid containers and squirted into culture tubes containing 13 cc. of liquid medium. Some of the medium was drawn back into the pipette in each case and used to wash the remaining yeast cells from the containers and pipettes. Thus, the final culture material consisted of 0.1 cc. of three day old culture in 13.9 cc. of fresh medium and 1 cc. of the test material in 13 cc. of fresh medium. These quantities were used to facilitate experimental manipulations and have no other significance.

# Measurement of Effect

As mentioned above the population density at various times was determined photometrically by measuring the amount of light transmitted through the medium containing organisms. The apparatus used consisted of four essential parts: (1) a fixed source of light with canalized beam; (2) a block to hold the culture tube properly in the beam; (3) a photoelectric cell; and (4) a milliammeter to measure the current generated by the light absorbed in the cell.

Before setting up the cultures, culture tubes were selected which gave the same milliampere reading on the instrument when placed in the holder with the Pyrex label always towards the operator. This tended to minimize peculiarities in readings due to irregular optical properties of the culture tube glass.

As is evident at the outset a constant light source is essential if consistent readings are to be had. Since electric current from an ordinary 110 volt alternating current outlet was used to

light the bulb and since a certain amount of line-variation seems inevitably to occur despite the use of a ballast tube, it was necessary to take certain precautions to insure reliable readings. To do this a tube of sterile medium was placed in the supporting block at the beginning and a reading taken. This was found to be near 350 microamperes. This figure was then adopted as a standard reference value and the instru-

## Results

Readings were taken twice daily, usually about 9 A.M. and 5 P.M. for about a week following irradiation, the specific time when the readings were made being recorded in each case. Results obtained would have been easier to handle if the readings had been taken routinely at the

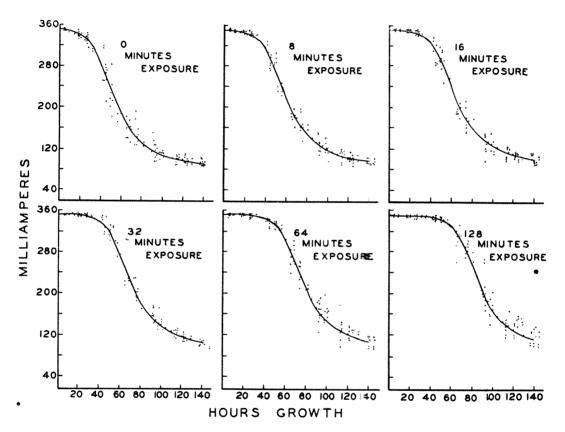


Fig. 1. Yeast growth curves after different exposures to roentgen rais and obtained with the photo-cell instrument. The abscissae show hours' growth following irradiation and the ordinates milliamperes read on the instrument. The curves have been drawn down to the level of 160 ma. in such a way that the horizontal separation between them is constant. Below this point they have been drawn to fit the experimental points in each case.

ment made to give this reading consistently both before and after every experimental reading. If any discrepancy was found the experimental value was discarded, the reference value of 350 again obtained by moving the support block (which is mounted on a rack and pinion carriage) nearer to or farther away from the light source and then a correct experimental value obtained.

same time each day. However, since the work at this point was largely exploratory in nature the importance of such procedure was not realized until after a number of experiments had been completed. Thus in order to avoid the necessity of presenting a complicated table of values and to allow the reproducibility of the experiments to be judged, all values have been plotted (Fig. 1).

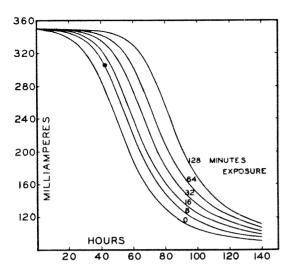


Fig. 2. A reproduction of the curves of Figure 1 in the same graph.

In Figure 1 the abscissae indicate hours growth following irradiation and the ordinates milliampere readings taken from the photo-cell instrument. Since the milliampere values become smaller as the number of organisms increases (growth), the downward trend of the curves indicates greater population density.

In an attempt to analyze the results a number of things were done. First of all the best possible smooth curves were drawn free hand through the points. From this alone it became evident that the curves were displaced to the right in accordance with the amount of radiation given and that they bore a strong resemblance to each other (better seen in Fig. 2).

In order to get a more definite idea of this resemblance, abscissae readings for corresponding ordinates were taken from all the curves. Examination of these disclosed that the abscissa distance from any one curve to another was practically the same at all levels. This interesting observation, if true, indicates that the growth, once manifest after treatment, continues at the same rate irrespective of the amount of radiation given.

To investigate this further, trial and error adjustments of the curves were made to see whether a set with constant horizontal differences could be made to fit the experimental points as well as any that could be drawn. The curves as drawn in Figures 1 and 2 bear such relationships to each other down to the level of 160. Below this, those for the more heavily irradiated material tend to become parallel with the abscissae somewhat more quickly. Accordingly the distances between the curves are slightly greater in this region. In any case, however, the deviations are small as may be seen in Figure 2. Since a constant difference is well manifest throughout the greater part of the curves and especially in the more significant region, it seems safe to say that for the most part the rate of growth of irradiated and non-irradiated organisms is the same once it becomes detectable—irrespective of the amount of radiation administered. The meaning of this will become more evident below.

The degree of separation between the curves of Figure 2 may be taken as a biological measure of irradiation effect. In accord with this, readings were made from the curves in the region where the slopes

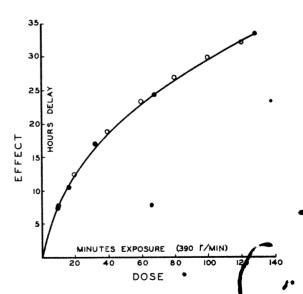


Fig. 3. Dose-effect curve showing hours' de ay in the onset of growth as a function of minutes exposure to roentgen rays. The closed circles represent experimental values whereas the open ones represent calculated ones (see text).

were the same and the differences calculated, taking the reading for the controls as zero. The data thus obtained are plotted in Figure 3 (closed circles). Figure 3, therefore, is a curve showing how the irradiation effect in terms of hours delay varies as a function of dose—a form of dose-effect curve.

As will be seen, the experimental points may be fitted with a smooth curve which rises rapidly at first and then more and more slowly. Before discussing this, however, let us return to Figure 2 and also present certain other tests.

It has been pointed out that the growth curves (Fig. 2) are displaced to the right in accord with the amount of radiation administered and that they are a constant distance apart over their significant range. Since we were measuring growth, the displacement indicates a delay in the onset of the growth process as detected with the photo-cell instrument. Consideration of the delay process caused us to undertake other experiments which have helped considerably in understanding the meaning of the dose-effect curve.

#### PART H

It became clear that delay in the onset of growth as indicated by the photo-cell measurements must have been caused in one of two ways by the radiation: (1) either by production of a physiological block thus causing the organisms to remain quiescent for varying periods of time following treatment, or (2) by certain organisms being killed outright by the radiation and others being unaffected.

Superficially, the first explanation seemed most satisfactory in view of the fact that organisms of this type sometimes tend to form inactive spores when unfavorable growing conditions are encountered. However, it was difficult to visualize how they could be quiescent at one moment and then at the text suddenly manifest the normal rate of growth, which is what appeared at first to be taking place.

By going back over the experimental

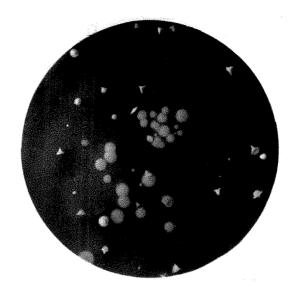


Fig. 4. Photograph showing the two characteristic forms of colony growth on agar plates (Saccharomyces cerevisiae, ×5).

conditions certain things were found which caused this explanation to seem less probable. It will be remembered that 350 milliamperes was the reading on the photo-cell instrument when a tube of sterile medium was used. Furthermore, it will be seen (Fig. 1) that a reading of 350 was also obtained when the tubes were freshly inoculated with test material and that this was true whether the material was irradiated or not. Thus, it was not possible to detect with the methods used whether organisms had been killed outright by the radiation or simply rendered quiescent for a period of time.

It was therefore decided to culture the organisms, both controls and irradiated, on agar plates in such a way that the resulting colonies could be observed. This was done to determine two things: (1) whether any organisms were killed outright by the irradiatiom; and (2) whether the colonies resulting from irradiated material developed any more slowly or showed any loss of vigor when compared with those resulting from non-irradiated material.

#### Procedure

Solid medium was prepared as described above and allowed to cool almost to the point

of gelation (approximately 42° C, which is about 3-4 degrees above the gelation temperature). One cubic centimeter of the test material was transferred to the center of a Petri dish by means of a sterile pipette. About 10 cc. of sterile agar medium (as prepared above) was poured directly over the culture and the plate rotated gently to insure a uniform distribution of the organisms throughout the medium. The medium was then allowed to solidify before being inverted and put away in the incubator at 26° C. After four days the colonies of organisms appear on the plates as shown in Figure 4. While the photograph shows a magnification of several diameters (4-5) the colonies may easily be seen and counted with the unaided eve.

The dilutions were such in this procedure that the colonies which arose in the culture dishes came from individual yeast organisms or colonies consisting of a few cells (see Figs. 8 and 10, Part IV). The colonies which developed were of two kinds as is characteristic of this form, a diffused type with smooth outline and an irregular type with a varying number of fantastic projections. Pure cultures of either type give rise to both smooth and irregular shaped colonies, both of which can clearly be seen in the photograph (Fig. 4).

The response of the organisms to irradiation when the plating procedure was used is shown in Figure 5. Going from left to right the test samples received respectively 0, 16, 32, 64 and 128 minutes' exposure to the radiation described above. The top row of plates was inoculated with one-tenth as many organisms as in the bottom row.

It will be seen first that there are consistently more colonies appearing in the dishes in the bottom row which is in accord with the dilutions made. A direct count of all the colonies present in corresponding pairs of plates shows the number in the top row to be approximately one-tenth that in the bottom row. Second, it will be seen, passing from left to right, that there are fewer and fewer colonies, the number thus dropping off in accord with the amount of radiation administered. Third, the size of the colonies appears not to be affected in any significant way by the irradiation, those in the heavily irradiated samples being fully as large as the largest of those in the non-irradiated. It will be seen that the colonies in the more concentrated samples are generally smaller—a condition well known to be associated with crowding. This, however, does not interfere with statement number three. These observations therefore yield answers to the points in question.

Finding fewer and fewer colonies in the samples receiving increasing amounts of exposure showed clearly that the delay indicated by the curves above is not due to a block in growth activity but to the outright killing of some of the cells. Furthermore, finding that the size of the colonies was in no way made smaller indicates that the vitality of the living forms was not appreciably, if any, diminished or impaired by the irradiation. This manifestation of unimpaired vitality is in accord with the photo-cell observations above, indicating that the rate of growth of the organisms remains the same irrespective of the amount of radiation applied.

Turning again to the dose-effect curve (Fig. 3), it will be recalled that this is a plot of values representing the horizontal distances between the curve for control material and those for the irradiated (Fig. 2). Since it has just been indicated that these distances result from a decrease in the number of viable organisms in the irradiated samples, it becomes clear that the dose-effect curve is actually a type of mortality curve—one showing in some way the relative number of organisms killed as a function of the amount of radiation administered.

The dose-effect curve may now be analyzed in the light of this and other conclusions thus far formulated.

Two significant characteristics of the curve are apparent at the outset. (1) It rises abruptly at the beginning and (2) its slope becomes less and less. It is therefore in striking contrast to the "S" or skew type killing curve obtained by the previous investigators. The abrupt rise indicates that no appreciable threshold dose is required before some manifestation of effect is apparent, and the decrease in slope that fewer and fewer organisms are killed per unit quantity of radiation as the dose is increased. In regard to the latter, it may be said that since the total number of organisms killed increases continually with dose, the dropping off of killing action may be correlated with the decreasein number of viable organisms present. Thus, it would appear that as the concentration of living forms becomes diminished, the number of organisms killed per unit quantity of radiation administered also is diminished. Considering then the fact that radiant energy is absorbed as discrete units or quanta, the loss in effectiveness of the radiation (per unit quantity) ma

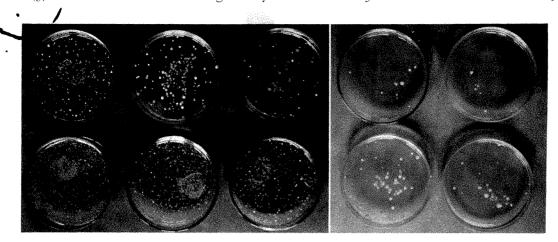


Fig. 5. Agar plate cultures of Saccharomyces cerevisiae showing different dilutions and the growth following varying exposures to radiation. The plates in the upper row had an original concentration one-tenth that of the ones in the lower row. Going from left to right the plates in both rows received respectively 0, 8, 16, 32, 64 and 128 minutes' exposure to roentgen rays (390 r/min.). Three significant things may be noted: (1) that the colonies in the more densely populated dishes are smaller whether receiving radiation or not; (2) that the colonies appear to be unaffected by the irradiation and (3) that the number of colonies present becomes less as the dosage of radiation administered is increased.

be attributed to the decrease in probability of encounters of energy quanta with photosensitive receptors in the organisms.

The curve (Fig. 3) was tested to determine whether it is of the exponential type, the type which would be expected if the action observed were due to the probable encounters of energy quanta with photosensitive parts in remaining viable organisms. The expression  $e^{ky} = ax + b$  was used for this purpose. The open circle points (Fig. 3) were thus obtained when k = 0.0678, a = 0.065 and b = 1. The points will be seen to lie on or very close to the experimental curve.

It is to be noted, however, that any slight shift in the position of a curve in Figure 1 (which might easily occur if more experiments were carried out) would cause a change in the curve (Fig. 3). Because of this, it seemed advisable to carry out a different kind of experiment in order that further information on the meaning of the results here might be obtained.

## PART III

In order to obtain a more direct measure of the killing rate produced by the irradiation, a survival curve was derived by making plate counts of colonies arising from samples given different amounts of radiation. More precisely, counts were made of colonies found in cultures treated and prepared as shown in the upper part of Figure 5. Seven such counts have been made on different preparations of material and the results are shown in Table 1. Since com-

TABLE I
YEAST PLATE COUNT EXPERIMENTS

1	EASI P	LAILC	OUNIE	XPERIN	4ENTS	
Minutes Exposed	0	8	16	32	64	128
Experi-		The state of the s	THE SOUTH STREET, SAME IS NOT STREET,	**************************************	784	The second of the same second
ment No.						
1	327	271	248	232	185	110
2	239	201	187	140	122	88
3	163	150	139	121	103	66
4	216	198	148	136	104	-
5	236	203	172	148	109	88
6	430	294	240	210	171	98
7	204	165	156	132	97	55
		Per	centag	e	•	
I	100	8.3	76	71	57	34
2	100	84	78	59	51	37
3	100	92	85	74	63	42
4	100	92	69	63	48	***************************************
5	100	86	73	63	46	37
6	100	68	56	49	40	23
7	100	81	76	65	48	27
Av.	100	84	~ · ·	62	70	3.3

pletely new material was used in each preparation, it was possible to have only approximately the same concentration of organisms at the beginning in each case. This, in the main, accounts for the differences in cell number of the controls and corresponding experimental samples as shown in the table (upper part). This, however, does not interfere with the investigation for the percentages run generally the same as may be seen in the lower part of the

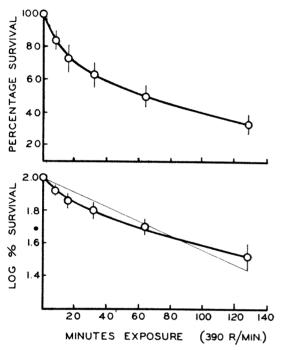


Fig. 6. Dose-effect curves showing percentage surviving (ordinates) as a function of roentgen-ray dosage (abscissae). The upper part shows the percentage surviving plotted in the usual way, whereas the lower part shows it plotted as logarithms.

table. Averaged percentage values, together with their standard deviations  $(\sigma)$  have been calculated and plotted in Figure 6 (upper part).

Examination of the curve indicates, as before, that no significant threshold dose of radiation is required before an effect begins to be manifest and also that the curve is of the die-away type. In the lower part of the figure, logarithms of the averaged values have been plotted. It will be seen in this case that the best curve through

the points tends to dip, but that a straight line may be drawn which falls almost within the limits of the standard deviations. The regularity of the points with respect to each other, however, is such that doubt is cast on the possibility that the curve is exponential. This, nevertheless, may be said: the deviation from the strictly exponential form is in a direction to avoid all confusion on the question of a threshold effect. Certainly there is not the slightest possibility that the curve is of the skew type.

#### PART IV

At this point an odd question enters in. It will be remembered, and it will become very apparent below, that the yeast forms were irradiated not only as single cells but also as groups or clusters of cells. Thus, since presumably every mature cell is capable of independent existence, it is difficult to understand how single radiation quanta can, as indicated above, produce killing in the multicellular forms unless death in a single cell causes death in all the cells of a colony.

To investigate this, certain microscopical examinations were carried out.

The first of these was a vital staining experiment with methylene blue. When this stain is applied properly, the living cells can usually be distinguished from the nonliving since only the non-living ones tend to take up the dye. Briefly, it was found that exposure to large doses of radiation did not change the appearance of the organisms appreciably so far as their ability to take up stain was concerned. Occasional stained cells were observed, but they occurred equally as often among the treated and non-treated samples. Following exposure, those colonies which fail to develop do not take up the blue stain as do those that have been killed by boiling or fixation. In general, they show no change whatso ever for several days while the developink forms undergo extensive proliferation. The methylene blue technique, therefore, fails to indicate that the yeast cells are killed

individually by the radiation and leads to the presumption not only that the colonies respond as units but that their death does not occur for some time after they have lost the power of proliferation. Actual proof of this, however, has not been obtained as

Parenthetically, we may describe here the photograph (Fig. 7) which shows something of the rate of proliferation in the yeast cells under normal conditions. While this point does not have a direct bearing on the question being discussed, it is one that

vet.

hours for the experimental conditions. At best, this figure can be only an approximation, for different cell groups may differ significantly in their proliferative rates, but it gives some idea of the division time.

Other microscopical examinations were carried out to compare the appearance of the irradiated and non-irradiated materials. This, in part, was a further attempt to determine whether any damage occurred in organisms surviving large doses of radiation. Figure 8 shows a series of photographs of both non-irradiated and irradiated forms,

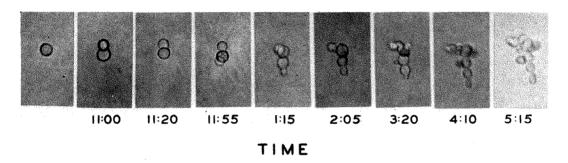


Fig. 7. Photographic series showing the growth of a yeast colony (see text).

invariably comes to mind when pondering the mechanism of action here. A fresh plate culture was prepared about 9 o'clock on the day photographs were to be made. A single cell was found and photographed as shown at the beginning of the series. At 11:00 o'clock two cells were observed as shown. Considering now the daughter cell, it was found to have a beginning bud at 11:20. If the bud be followed in the photographic series, it will be found to have matured and produced a similar bud by 2:05—slightly more than two hours. Several instances of this kind may be found in the series and the division interval seems to range from a few minutes less than two hours to a few minutes more than this gure for the conditions used. As mainained under the microscope in an enclosed anging drop of solidified agar, the culture vas kept at a temperature 3–4 degrees below the usual culture temperature of p° C. Accordingly, the time for division as undoubtedly somewhat less than two

the latter having been exposed to 25,000 roentgens (64 min., 390 r/min.). The photographs were made twenty-four hours after the treatment and plating procedure had been completed. Figure 9, likewise, shows similar materials 120 hours after treatment and culture. The specimens shown were selected to show that colonies of all sizes are present in both irradiated and control samples. Moreover, it will be seen that there is no significant difference in the appearance of the two kinds of material. Subcultures prepared of both irradiated and non-irradiated materials taken from the large colonies grow identically as nearly as can be ascertained. The findings, therefore, bear out the observations above that colonies which survive the radiation treatment appear to behave as though they had received no treatment at all.

While colonies of all sizes were found in both treated and untreated samples, the photographs (Figs. 8 and 9) show nothing of the frequency of occurrence of colonies

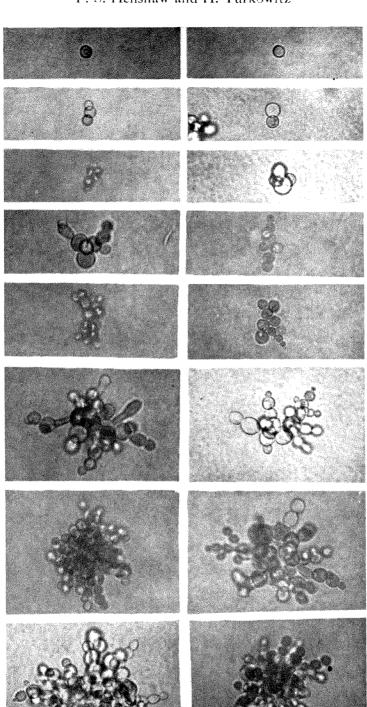


Fig. 8. Photographic series showing the lack of visible irradiation effect on colonies of different sizes. T photographs were taken twenty-four hours after treatment and seeding into the agar plates. (×400

CONTROLS

IRRADIATED

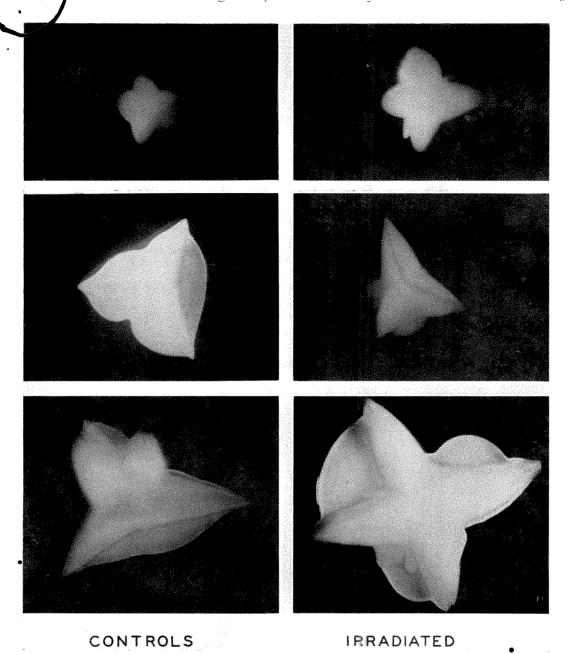


Fig. 9. Same as Figure 8, 120 hours after treatment and seeding ( $\times$ 15).

of different sizes. To obtain an idea of this, founts were made of the number of cells per colony in a large number of colonies selected at random. This was done for irridiated and non-irradiated material and for material of different ages. One to two hundred colonies were counted for each condition considered in five different sets

of experiments. The averaged results are shown in Figure 10. The classes used (2, 3, 4–5, 6–8, 9–12, 13–17, 18–25, 26–40 and 41–cells) were selected arbitrarily to facilitate counting since in the large colonies it was sometimes difficult to be certain of the precise number of cells and also to make the results more manageable. A good many

single cells (perhaps 5–10 per cent) were present but since it was easy to confuse these with artefacts in the medium (small bubbles), the were simply omitted from the consideration.

Examining Figure 10, it will be seen that at the time of culturing, no colonies had more than twenty-five cells and that most of them had less than eight; this was true both for irradiated and non-irradiated ma-

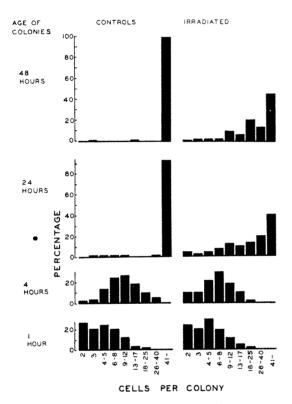


Fig. 10. Chart showing the frequency of colony size with respect to cell number for irradiated and non-irradiated materials at different times after treatment and seeding into the agar plates.

terials. Within four hours, however, a definite shift had occurred in both, this perhaps being a little greater for the controls. By the end of twenty-four hours more than 90 per cent of the controls had become colonies of more than forty cells whereas only about 40 to 45 per cent of the irradiated colonies had reached this stage, those not reaching it being distributed among all the lower classes. By the end of

forty-eight hours this picture had not changed appreciably so far as this classification was concerned.

Close examination of the results shows that about 45 per cent of the irradiated colonies reach the forty-cell stage. This value becomes especially interesting when it is noted in Figure 6 that the percentage of colonies developing to the point of visability (with the unaided eye) is about fifty for samples receiving the same treatment of 25,000 r and the same handling. The two values, therefore, are significantly close together and indicate that if irradiation damage is produced in the colonies by the irradiation, they seldom, if ever, go beyond the forty-cell stage. It is clear from these findings, therefore, that some but only a small amount of proliferation follows the effective action of irradiation on the cells.

#### DISCUSSION

The results presented here differ in certain respects from those of Holweck and Lacassagne and of Wyckoff and Luyet:
(1) whereas they observed immediate killing, we observed several cell divisions among those cells (or colonies) which died as a result of exposure to radiation;
(2) whereas they observed partial injury, we observed only complete killing; and
(3) whereas their dose-effect curves, for all radiations used, showed a significant threshold dose, ours indicated none.

The first two discrepancies, however, seem more apparent than real when the different criteria of effect are taken into account. Holweck and Lacassagne divided the organisms affected by the radiation into three classes: one in which no cell division occurred, "immediate death";\* one in which a single division occurred, "deferred death"; and one in which more than a single division occurred. Wykoff and Luye likewise used these criteria but in addition classified the colonies formed as to number of cells up to the eight-cell stage. We, on the other hand, allowed the cells that would

<sup>\*</sup> Single cells (not colonies) being inferred for the beginning of the experiment.

o form colonies and by following closely what happened found that colonies of more than eight cells may be reached before death from irradiation occurs. Thus, it would seem that the previous investigators might have observed a greater percentage of killing in the total population if a longer period of development had been allowed. Holweck and Lacassagne, in fact, state that the proportion of the three classes of abnormalities changed with time.

Because we have found that irradiated colonies which survive to the forty-cell stage grow normally and manifest no detectable injury, we are able to emphasize the all-or-none action of irradiation on yeast and that the reason why the previous workers observe partial injury was probably because the irradiation effect was not fully manifest when measured.

The third point, difference in shape of survival curves, is more difficult to deal with. In view of the fact that we are here working with an affecting agent consisting of discrete quanta, a test object made up of individual cells (or colonies) and a response that is complete killing, the shape of the survival curves, as mentioned above, may be taken to indicate certain basic characteristics of the reaction in progress. Thus the difference between our curves and those of the previous investigators is a matter of importance.

Two factors may be mentioned in this connection: (1) species of organism used, and (2) wave length of radiation used.

It seems unlikely, however, that the differences observed can be attributed to species of organism used for although Holweck and Lacassagne used S. ellipsoideus, Wyckoff and Luyet used S. cerevisiae as did we. By default, therefore, the matter of vave length dependence comes to the fore. Interpreted on this basis, the difference between the non-sigmoid curves obtained by us and the sigmoid ones obtained previously must be taken to mean that somewhere along the wave length scale between the quality of radiation used by us and that used by the previous workers, the

reaction changes from the one-hit-to-kill type to that of the multiple-hit-to-kill. Although this seems the most likely interpretation at present, we are unwilling to accept it. This unwillingness is due largely to questions arising in connection with the colonial character of the organisms at the time of treatment. The results in Part IV above indicate that death in a single cell causes death in the colony of which it may be a part. While this finding is consistent with the shape of the curves obtained, it is not consistent with what has been believed in connection with the biology of yeasts. To investigate the shape of the survival curve further, it seemed advisable to use a noncolony-forming species and thus eliminate the uncertainties associated with multicellular test objects. This avoids the interesting question of the influence of a damaged cell of a colony on the other cells of that colony, but seems to be the best procedure at present.

#### SUMMARY

- 1. Experiments have been carried out to investigate the action of roentgen rays on Saccharomyces cerevisiae. For the first work, the growth of samples receiving varying amounts of radiation was determined by measuring the turbidity of the suspensions with a photo-cell instrument. A family of curves was obtained which indicated that the growth processes were delayed in some way by the irradiation but not impaired by it.
- 2. The delay, plotted as a function of exposure to the radiation, gave a set of points that could be fitted well with an exponential type of curve.
- 3. Using the agar plate technique, the colonies arising from organisms receiving varying amounts of radiation were then followed. From this it was learned that the delay observed with the photo-cell instrument was due to organisms being killed by the irradiation rather than injured by it, and that those which survived appeared to be as vigorous as the controls. In regard to the latter, the organisms which survived

behaved as though they had received no treatment whatsoever.

- 4. Counts were made of the number of colonies arising from samples receiving varying amounts of radiation and a survival curve was plotted from the data obtained. This, likewise, tended toward the exponential type but some question arose in connection with the distribution of the experimental points. However, the complete lack of a sigmoid character in this curve and in the curve obtained with the photo-cell instrument, places the response of *S. cerevisiae* to 200 kv. roentgen rays in the one-hit-to-kill category.
- 5. Microscopical examinations showed that cells affected lethally may undergo several divisions following exposure, but that they rarely, if ever, go beyond the forty-cell (colony) stage.

We wish to express our appreciation to Dr. G. Failla for his interest and cooperation throughout the course of the work and for his suggestions.

#### REFERENCES

- BUCHTA, L. Ueber den Einfluss des Lichtes auf die Sprossung her Hefe. Centralbl. f. Bakteriol.,
   Abt., 1914, 41, 340-351.
- 2. Holweck, F., and Lacassagne, A. Sur le mécanisme de l'action cytocautique des radiations. *Compt. rend. Soc. de biol.*, 1930, 103, 766-768.
- 3. Holweck, F., and Lacassagne, A. Action sur les levures des rayons X mous (K du fer). Compt. rend. Soc. de biol., 1930, 103, 60-62.

- 4. Holweck, F. Étude energetique de biologique de diverses radiations. Compt. rend. Acad. d. sc., 1930, 190, 527-530.
- 5. KOERNICKE, M. Ueber die Wirkung von Röntgen- und Radiumstrahlen auf den pflanzlichen Organisms. *Ber. d. deutsch. botan. Gesellsch.*, 1904, 22, 148–166; 1905, 23, 404–414.
- LACASSAGNE, A. Difference de l'action biologique provoquée dans les levures par diverses radiations. Compt. rend. Acad. d. sc., 1930, 190, 524-526.
- LACASSAGNE, A., and HOLWECK, F. Sur la radiosensibilité de la levure Saccharomyces ellipsoideus. Compt. rend. Soc. de biol., 1930, 104, 1221-1223.
- 8. Nadson, G., and Philippov, G. Action excitante des rayons ultra-violets sur le développement des levures et des moisissures. *Compt. rend. Soc. de biol.*, 1928, 98, 366-368.
- 9. VON RECKLINGHAUSEN, M. J. Am. Waterworks
  Ass., 1914, 1, 565.
- 10. RICHARDS, Ö. W. Potentially unlimited multiplication of yeast with constant environment, and the limiting of growth by changing environment. J. General Physiol., 1928, 11, 525-538.
- 11. RICHARDS, O. W. The second cycle and subsequent growth of a population of yeast. *Arch. f. Protistentk.*, 1932, 78, 263-301.
- RICHARDS, O. W., and JAHN, T. L. A photoelectric nephelometer for estimating the population density of microörganisms. J. Bacteriol., 1933, 26, 385-391.
- 13. Wels, P., and Osann, M. Die Wirkung der Röntgenstrahlen auf die Hefezelle. Arch. f. d. ges. Physiol., 1925, 207, 156–164.
- WILLIAMS, R. J. Quantitative method for determination of vitamine. J. Biol. Chem., 1920, 42, 259-265.
- 15. WYCKOFF, R. W. G., and LUYET, B. J. Effects of x-rays, cathode, and ultra-violet rays on yeast. *Radiology*, 1931, 17, 1171-1175.



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# THE PRODUCTION OF RADIOACTIVE SUBSTANCES AND NEUTRON RAYS\*

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IT IS the purpose of this paper to tell something of the recent discoveries and techniques of physics which have given to medicine and biology new and powerful tools whose uses have been described in recent papers. In the limited space available it is necessary to make many statements quite dogmatically. The details of the experimental elucidation of the facts described here can be found in various excellent textbooks and summarizing articles which have appeared recently.

In the closing years of the nineteenth century a series of startling discoveries inaugurated a period of extreme fertility in the physical sciences. These were the discoveries of the electron, x-rays and radioactivity—all phenomena essentially atomic in character. In the next quarter of a century experimental physicists have demonstrated that the atom is a complicated structure consisting of a central body (the *nucleus*), in which nearly all the mass is concentrated, surrounded by one or more swiftly moving electrons. Such a model of the atom, like an infinitesimal solar system, is a very helpful one in visualizing many of its properties. It is a model, however, which is somewhat too simple and in the course of further development it has been found that this analogy cannot be stretched too far. The number of electrons surrounding the nucleus is the same for all the atoms of any one particular chemical element and varies for different ements. The number of electrons, therefore, determines the chemical characteristics of any particular atom, and because of this great importance has been given the name aromic number. It has also been found that electricity is also essentially atomic in that no electrical charge smaller than is carried by one electron has ever been found. Since normally an atom is electrically neutral, the nucleus must carry an electrical charge equal and opposite to the total charge of the surrounding electrons. The circumnuclear electrons are negatively charged and consequently the nucleus must be positively charged.

The mass of the nucleus is, in round numbers, the atomic weight of the atom. When a chemist measures the atomic weight of an element he is measuring an average of the atomic weights of the various atoms which make up the chemical weight of an element. By this, one must understand that all the atoms of a chemical element do not have the same weight even though they have the same number of surrounding electrons. Thus, chlorine has a chemical atomic weight of 35.457 and is actually made up of two kinds of chemically identical atoms. About 75 per cent of these have a mass of 35 and 25 per cent have a mass of 37. Since the atoms are chemically identical, their outer appearance must be the same. On current views of chemical combination we understand that the chemical properties of an atom depend on the outer electronic structure, and consequently two different nuclei with the same electrical charge will surround themselves with the same number of electrons and will be chemically identical. Such atoms are called isotopes.

From these remarks it is obvious that

<sup>&</sup>lt;sup>1</sup> Lawrence, John. Handbook of Physical Therapy. American Nedical Association.

Feather, N. Nuclear Physics, Cambridge University Press, 136. Rasetti, F. Elements of Nuclear Physics, Prentice-Hall, 136. Lord Rutherford, The New Alchemy. Bethe, H. A. Reviews Modern Physics, April, 1936, April, 1937, July, 1937.

Read at the Twenty-Third Annual Meeting, American Radium Society, San Francisco, Calif., June 13-14, 1938.

from the infinite variety of nuclei which we could imagine as having been born in the chaos of creation, only a certain limited number of these have survived on the earth to this day. The ones which did not survive must have represented types which were poorly constructed—they were either too light or too heavy and in the long periods of geologic time those with an unsound architecture have fallen to pieces or disintegrated. This view is further strengthened by the fact that some of these prehistoric monsters actually have survived. All the heavy, naturally radioactive elements such as uranium, thorium and radium belong to this class. It is an everyday experience for a physicist to observe and study the disintegration of these elements since they express their instability by the emission of radiations. Several varieties of these radiations are known and are used daily by medical men. Some nuclei disintegrate by emitting high speed alpha particles (which are identical with the nuclei of helium atoms) others by the emission of beta particles (which are simply swiftly moving electrons). The emission of alpha and beta particles are often accompanied by the emission of gamma rays (similar to but harder than roentgen rays). It is very easy to detect radiations of this type and therefore to find out how many atoms of, say, one gram of uranium are disintegrated per second. This is a very large number, but compared to the number of atoms in the gram of uranium it is sufficiently small for us to understand how uranium has lasted. Indeed, one of the best ways of estimating the age of the earth is from just such measurements as this.

Since the discovery of the *neutron* seven years ago physicists have learned that all nuclei are built up of neutrons and *protons*. The proton is an old friend, having been known for over twenty years, and is simply the nucleus of an ordinary hydrogen atom. It has been found that a neutron has no electrical charge and a proton has a unit positive charge. The charge on the proton

then is equal and opposite to the charge of an electron. The proton and neutron have almost identically the same mass and are each about 1,850 times as heavy as an electron. A single proton will attract to itself a single electron forming a hydrogen atom. A combination of one neutron and one proton will also attract to itself a single electron and this will, of course, be chemically indistinguishable from an ordinary hydrogen atom. It will, however, be twice as heavy. The heavy isotope of hydrogen is well known and can be bought pure as a compressed gas in cylinders. It is called deuterium and its nucleus is the deuteron. A combination of two neutrons and two protons, together with two surrounding electrons, constitutes a helium atom. The nucleus of helium is the alpha particle, is extremely stable, and acts as a secondary building block in nuclei.

To recapitulate: our present idea of the construction of an atom is that it consists of a nucleus surrounded by a certain number of electrons. The number depends upon the chemical properties of the atom. The nucleus has exactly the same electrical charge as the total charge of the electrons. but of opposite sign. The nucleus, too, is composite, being composed of the same number of protons as there are electrons outside and a number of neutrons necessary to give it the proper mass. In the example given above the two kinds of chlorine atoms would be denoted by the symbols Cl35 and Cl37. Chlorine has an atomic number of 17, therefore has 17 electrons around its nucleus. The latter has 17 protons and 18 neutrons for Cl35 or 20 neutrons for Cl<sup>37</sup>.

When high speed particles or other radiations pass through solid matter, the effects they produce vary markedly from one to another. Thus swift alpha particles or protons are easily stopped in a fraction of a millimeter of any solid body. This is because of the strong electrical forces between them and the electrons of the atoms composing the solid matter. Because of their smaller mass electrons are slightly

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more penetrating. Roentgen rays and gamma rays are much more penetrating. In addition, they have the property of ejecting electrons from the atoms through which they pass. The biological action of these rays is entirely due to these secondary electrons. When neutrons pass through matter they, having no electrical charge, are not clutched at by the electrons of the ambient atoms and so are very penetrating. Only when a neutron strikes a nucleus is it slowed down. Even then the slowing down is small unless the atom is a hydrogen atom. The neutron simply bounces off the heavier nuclei of lead, iron, copper, etc. The cue ball on a billiard table is not greatly slowed down when it bounces off the rail, but soon loses speed when it makes frequent collisions with other balls whose mass is the same as the cue ball. The situation is similar with neutrons-hydrogenrich substances like water and paraffin are the best absorbers. The biological action of neutrons is due to the destructive action of the knocked-on protons which accompany its path through biological material. That this is much greater than that of roentgen rays is traceable to the much greater destructive ability of a swift secondary proton as compared with a swift secondary electron.

If, now, we admit that only a certain group of all the possible nuclei, which we could imagine as being formed by combinations of neutrons and protons, will be stable, then we must imagine that if by any means whatever we can force two nuclei to coalesce, such as by firing one nucleus at the other at high speed, the resulting composite may break up into two or more nuclei. It may be that these two will be identical with the original nuclei and we cannot tell whether they we coalesced or simply bounced off each ther. It may be that the two or more nyclei will be different from either of the ntial nuclei and we will call this a transnutation. A great many of these transmutations have been accomplished and are such a commonplace of nuclear physics

that they are treated very much as chemical reactions except that only by analogy are they similar to the usual chemical reaction. Thus, the reaction:

$$N^{14} + He^4 = O^{17} + H^1$$

means that alpha particles (He<sup>4</sup>) have been shot into nitrogen (N<sup>14</sup>) and have caused a transmutation in which a proton (H<sup>1</sup>) is ejected and a heavy atom of oxygen remains. The superscripts attached to the chemical symbols indicate which isotope of that particular element is being referred to. Nitrogen has two isotopes of masses 14 and 15 of which the lighter predominates. Oxygen has three of masses 16, 17 and 18 of which 16 predominates. The isotope of mass 17 was discovered in the earth's atmosphere several years after it was proved conclusively that it had been made in this experiment.

Since all nuclei have a positive charge they repel each other with enormous forces and in general it is only when the energy with which nuclei are shot together is of the order of a million volts that reactions such as the one above take place. A limited number of such transmutations were discovered using the high-speed alpha particles emitted by radium and its products. Realizing the limited efficacy of these natural particles physicists went to work to devise artificial means of accelerating nuclei to high speeds. With these artificially accelerated projectiles a great many more transmutations were exposed. Other projectiles besides alpha particles were tried, of which one of the most successful was the deuteron.3

It was later discovered that occasionally one of the nuclei resulting from a transmutation was different from any of the known stable isotopes. Thus, a reaction took place when aluminum was bombarded by alpha particles as indicated by the following equation:

$$Al^{27} + He^4 = P^{30} + n^1$$

Several months earlier the neutrons result-

<sup>&</sup>lt;sup>3</sup> Lewis, Livingston and Lawrence. Phys. Rev., 1933, 44, 55. Lawrence, Livingston and Lewis. Phys. Rev., 1933, 44, 56.

ing from this disintegration had been observed. It had also been observed that positive electrons were also emitted during this disintegration. There was considerable mystery about this for a while before the exact nature of what was going on was discovered. In the first place, it was reasoned that since aluminum and phosphorus have only one isotope something like this must be happening. Furthermore, the positive electron was a newcomer with which people did not feel completely familiar and some thought that the reaction

$$Al^{27} + He^4 = Si^{30} + H^1$$

was occurring, and that somehow the proton was breaking up into a neutron and positive electron on its way out of the nucleus. The astonishing fact was that when the alpha-particle bombardment was stopped positive electrons kept on coming. The number which emerged dropped to half its initial value in two and one-half minutes, to one-quarter of its initial value in five minutes, to one-eighth of its initial value in seven and one-half minutes. If the aluminum was dissolved and a chemical separation for phosphorus made, the positive electrons were found to come from the phosphorus precipitate. By a series of tests like this it was established that the first equation was the correct one, and that the experiment had consisted in creating a new nucleus (P30-ordinary phosphorus has a single isotope of mass 31). It was also clear why this nucleus was not found on the earth because it disintegrated so rapidly that in the course of a few hours none of it would be left. This subsequent disintegration can be expressed in an equation as follows:

$$P^{30} = Si^{30} + e^{+}$$

where e<sup>+</sup> stands for the positive electron. It was thus made possible to create new atoms which differed in no way from ordinary chemical atoms except for the fact that their nuclei were unstable and emitted penetrating radiations whose hardness was as great or greater than those of the natural radioactive substances. This phenatural radioactive substances.

nomenon is known as the production of artificial radioactivity. It has since been found possible to manufacture more new unstable radioactive elements than there are stable elements. Moreover, it is possible to manufacture them with activities in the neighborhood of that of a gram of radium.

Due to the ease with which the radiations from such artificially produced radioactive substances can be detected even through fair thicknesses of biological material, they have already come into considerable use as tracer elements in metabolism studies as has already been indicated by other papers.<sup>4</sup> It must here again be emphasized that the chemical properties of these radio-elements differ in no way from the chemical properties of their stable sisters.

A great variety of devices have been constructed to speed up atomic particles to such a degree that they may be able to cause transmutations. Of these the most successful so far has been a device known as the *cyclotron*, invented by E. O. Lawrence.<sup>5</sup>

In common with all instruments for acclerating atomic particles the cyclotron makes use of the fact that electrically charged atoms can be accelerated by an electrical field. There are many means of charging or ionizing atoms. In Figure 1 let us assume that there are a large number of ions of the particular sort we wish to accelerate at the point P which is at the center of a large, cyclindrical, air-tight, brass box. In the interior of this brass box are two electrodes A and B made of copper and having a shape very much like half of a pill box. These electrodes are connected to a radiofrequency oscillator so that they are driven alternately positive and negative several million times a second. If the ion is positively charged it will be pulled toward A when A is negatively charged.

8 Lawrence and Cooksey. Phys. Rev., 1936, 50, 1131. Kdrie. J. Applied Physics, 1938, 9, 691.

<sup>&</sup>lt;sup>4</sup> See reference 1 and the following as examples: Chiev tz, O., and Hevesy, G. Det. Kgl. Danske Videnskabernes Selsab. Biolog. Meddelelser x111, 9 (1937). Hamilton, J. G. Proc. Sat. Acad., 1937, 23, 521.

If now a large, steady magnetic field is applied perpendicular to the box (and to the plane of the drawing) the ion will be forced to move in a circular path so that after a very short time the ion will return to the gap between the electrodes. If it arrives at the gap in time to find that the charge on A has reversed it will be repelled from A and consequently gain in speed. The size of the circle in which it travels will now be a little greater but the time

D, pulls the ion away from the center and directs it toward a thin window, W, through which it passes into the outside world.

It is this stream of high-speed ions which has the ability to transmute elements placed in its path. Its ability to transmute depends on both its energy and the atomic number of the element being bombarded. The great preëminence of the cyclotron is due entirely to its being the only instru-

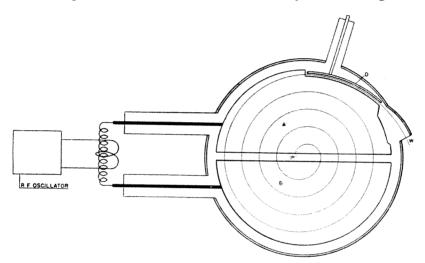


Fig. 1. Schematic diagram of the essential parts of the cyclotron. This represents a cross section of a flat, hollow brass box which is placed between the poles of a strong electromagnet. Inside the box are two D-shaped electrodes between which an electric field is caused to escillate very rapidly by means of the radiofrequency oscillator shown coupled to the electrode supports at the left. An ion created at P will follow a spiral path as shown, until it eventually emerges through the window W to be utilized as described in the text. (Republished, with permission, from General Electric Review.)

taken for the ion to describe a semicircle will be unchanged so that the ion will swing around crossing the gap in step with the oscillating electrical field so that each time it gains velocity. Obviously, if the maximum potential difference between the electrodes is 100,000 volts the ion will be accelerated to 10,000,000 volts after crossing the gap a hundred times. These repeated accelerations cause the ion to spiral from the center of the apparatus toward the periphery, so that when it attains the relaximum energy which the size of the electrodes will allow, it can escape into a region where an electrically charged plate,

ment whereby high-speed ions with energies in excess of 2 million volts have been produced. It is a matter of no particular difficulty to accelerate particles until they have an energy of over 10 million volts. Several cyclotrons are now being constructed which will give particles with an energy of between 15 and 25 million volts.

Apart from the fact that any artificial accelerating device can emit particles of a great many different kinds in contrast to the one kind emitted by naturally radioactive sources and thereby cause transmutations which could not be attained with alpha particles alone, it is interesting to

compare the intensity of the radiation from the cyclotron with that from natural radioactive sources. The number of highspeed particles emitted per second from a cyclotron is usually measured in microamperes. If these particles are singly charged (protons or deuterons) one microampere represents the total number of alpha particles emitted by 40 grams of radium. This is about one-twentieth of the total supply of radium in hospitals, laboratories, etc., in the whole world. A comparatively small cyclotron (such as the 37-inch installation at the University of California) can easily produce about 80 microamperes at 8 million volts. The new 60-inch cyclotron at the University of California which has recently been completed has been able to produce many times these numbers. With the 37-inch cyclotron it is, for example, possible to make 70 millicuries of radiosodium per hour. Thus, in a good long day's work, a radioactive sample as strong as one gram of radium can be made. The artificial radioactive sources are, with good technique, every bit as concentrated as radium itself. Since one millicurie represents the activity of one milligram of radium, the fact that radiophosphorus samples have been prepared with a strength of 36 millicuries per milligram of phosphorus is an eloquent demonstration of this.

The production of neutrons is simply another type of transmutation in which some substance is bombarded by high speed particles. The most prolific nuclear reaction thus far known is the bombardment of beryllium with swift deuterons in accordance with the reaction:

$$Be^9 + H^2 = B^{10} + n^1$$

With 80 microamperes of 8 million volt deuterons the yield of neutrons is sufficiently great to give a tissue dose comparable to that from a standard treatment roentgen-ray tube. A neutron dose is frequently measured in n units instead of the familiar roentgen. At 70 cm. skin-target distance and with a 3 cm. lead filter the 37-inch Berkelev cyclotron gives 240 n per hour; 200-250 n gives a skin reaction similar to that following 1,300 r of 200 kv. x-rays. One n-unit is equivalent to about 2.5 r x-rays in tissue ionization, and according to present experimental evidence is about six times as biologically effective as I r of x-rays.

Recent improvements in cyclotron technique have been responsible for great increases in the yield of both radioactive materials and neutron rays. The figures given in this paper by no means represent the ultimate yield of the instrument.



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Twenty-fifth Annual Meeting: New York City, June 10-11, 1940.

#### ~ E D I T O R I A L »

#### FIBROCYSTIC DISEASE OF BONE

POLLOWING the demonstration of the relation existing between disturbances of the parathyroids and the diffuse fibrocystic disease of bone, often referred to as von Recklinghausen's disease, a great deal of attention has been given to the recognition of these cases and to the benefit which might be derived from parathyroidectomy. These studies were greatly stimulated by those of Aub and Hunter, particularly their work on calcium and phosphorus metabolism in relation to fibrocystic disease, and as a result a widespread interest in cystic disease of bone in general has been awakened.

Out of all of this maze of reports and investigation it has been clearly demonstrated that not all of the diffuse cystic changes in the skeleton are due to parathyroid disturbances and not all of them are benefited by parathyroidectomy. Wilder and Howell, from a study of 135 proved cases, gave the following as the invariable features of this group which apparently are not associated with parathyroid disease as an etiological factor: In order to make an indisputable diagnosis of osteitis fibrosa cystica there must be the skeletal appearances typical of this disease; there must be indisputable abnormality of calcium metabolism demonstrated by a study of the blood or urine, and there must be tumorous enlargement of one or more parathyroids. Later, however, Gutman and his coworkers suggested that evidence of disturbed calcium metabolism will not necessarily always accompany even true fibrocystic disease of the skeleton associated with parathyroid tumor. They pointed out that a normal blood calcium figure may often be found in such cases in the presence of renal failure and that from experimental evidence variations in calcium intake may

possibly be of importance and also that the disease may be subject to spontaneous remissions.

Hunter some time ago pointed out that roentgenographically there are skeletal changes simulating osteitis fibrosa cystica where there is a multiple focal type of fibrocystic disease and that these skeletal changes may occur without parathyroid tumor.

Recently Robson and Todd<sup>1</sup> reported a case of fibrocystic disease of bone with extensive skin pigmentation and endocrine dysfunction. Previous to the reports of Robson and Todd, Albright and others described a syndrome characterized by osteitis fibrosa disseminata with areas of skin pigmentation and endocrine dysfunction with precocious puberty in females and in none of the cases which Albright reported was there evidence of a parathyroid tumor. The cases reported by Albright, Robson and Todd, and others, have as the chief feature of their syndrome an extensive osseous dystrophy of the fibrocystic type, either generalized or unilateral, pigmentation of the skin and in girls precocious sexual development. The clinical picture has a striking resemblance to hyperparathyroidism, though there is no negative calcium balance and in exploration of some of these cases no parathyroid tumors have been found.

The roentgenographic appearance of the skeleton, particularly in advanced cases, is indistinguishable from that seen in true types of fibrocystic disease of bone associated with hyperparathyroidism. One striking characteristic of the skeletal changes is the tendency to a unilateral involvement of the skeleton.

<sup>&</sup>lt;sup>1</sup> Robson, K., and Todd, J. W. Fibrocystic disease of bone, Lancet, 1939, 1, 377-380.

Robson and Todd, in a discussion of their case which bore great similarity to previous cases reported, suggested that the bizarre association of bone changes with cutaneous pigmentation and precocious puberty in the females might point to the condition being a specific entity and that possibly the male cases, in which no precocious puberty occurs, should be regarded as distinct from the female.

McCune and Bruch<sup>2</sup> reported a case of a Jewish girl of nine who exhibited true precocious puberty, asymmetrically tributed fibrocystic osteodystrophy of a progressively incapacitating nature and unchanging pathologic pigmentation of the skin. These features had been manifested in their case since the second year of the patient's life. The plasma phosphatase activity was increased; in other respects, however, numerous clinical examinations of the blood gave normal results and the calcium and phosphorus metabolic studies gave findings similar to those obtained for healthy children. The patient showed no hypercalciuria, and biopsy of the bone provided no clearcut information concerning the precise classification or the etiology of the osseous dystrophy. In their studies they were able to gather from the literature and other sources eight, possibly nine, females with an identical condition and five males showing fibrocystic osteodystrophy and pathologic pigmentation of the skin but not precocious puberty and they concluded

<sup>2</sup> McCune, D. J., and Bruch, H. Osteodystrophia fibrosa. Am. J. Dis. Child., 1937, 54, 806-848.

that there is some question as to whether the condition of the males and that of the females are fundamentally related. These unusual skeletal changes associated with pigmentation of the skin and apparently unassociated with parathyroid tumor suggest an identical etiological factor but a careful study of all of the available evidence relating to the collected cases gives no exact information concerning the nature of the factor.

Braid,<sup>3</sup> who was probably the first to record such a condition in the male, advanced the opinion that the bone dystrophy is due to some impairment of the function of the liver, possibly a mechanism concerned with the storage and utilization of vitamins.

The striking clinical and roentgenological manifestations in these cases is a challenge to further study in order to arrive at the underlying etiological factor and all cases presenting such clinical and skeletal changes and demonstrated roentgenographically should be adequately studied and reported in the hope that in the accumulation of evidence there might be brought about an elucidation of the causal factor. Whether it is, as Braid suggests, liver disturbances concerned with the utilization of vitamins or a disease of endocrine imbalance remains to be proved. While it may be a clinical entity, its striking similarity in many respects to von Recklinghausen's disease cannot be denied.

<sup>3</sup> Osseous dystrophy following icterus neonatorum. Lancet, 1939, 2, 798.



#### SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

#### MEETINGS OF ROENTGEN SOCIETIES\*

United States of America

AMERICAN ROENTGEN RAY SOCIETY

Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Boston, Mass.,

Oct. 1-4, 1940.

AMERICAN COLLEGE OF RADIOLOGY

Secretary, Mac F. Cahal, 540 N. Michigan Ave.,
Chicago, Ill. Next Annual Meeting: New York City,

Section on Radiology, American Medical Association Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: New York City, June 10-14, 1940.

RADIOLOGICAL SOCIETY OF NORTH AMERICA Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting, 1940: To be announced.

RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SOCIETY Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September. Section on Radiology, Illinois State Medical Society Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill. Next meeting Peoria, Ill., May 21–23, 1940.

RADIOLOGICAL SECTION, Los ANGELES CO. MED. Soc. Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.
RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION

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BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY

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CHICAGO ROENTGEN SOCIETY

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CINCINNATI RADIOLOGICAL SOCIETY
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CLEVELAND RADIOLOGICAL SOCIETY

Secretary, Dr. H. A. Mahrer, 10515 Carnegie Ave. Meets at 6:30 P.M. at Mid-Day Club rooms on fourth Monday each month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB

Secretary, Dr. E. A. Schmidt, 4200 E. 9th Ave., Denver, Colo. Meets third Tuesday of each month.

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FLORIDA STATE RADIOLOGICAL SOCIETY

Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.
GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg.,

Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

ILLINOIS RADIOLOGICAL SOCIETY

Secretary, Dr. E. P. Halley, Decatur and Macon County Hospital, Decatur, Ill. Meetings held quarterly, time and place designated by president.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annuKENTUCKY RADIOLOGICAL SOCIETY

Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville. Meets annually in Louisville on third Sunday afternoon

LONG ISLAND RADIOLOGICAL SOCIETY

Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

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MINNESOTA RADIOLOGICAL SOCIETY

Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

NEBRASKA RADIOLOGICAL SOCIETY

Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets first Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY

Secretary, Dr. W. J. Marquis, 198 Clinton Ave, Newark. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by president.

NEW YORK ROENTGEN SOCIETY

Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY

Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY

Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November.

PACIFIC ROENTGEN CLUB

Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY

Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Annual meeting, June, 1940, exact time and place to be decided.

PHILADELPHIA ROENTGEN RAY SOCIETY

Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St

PITTSBURGH ROENTGEN SOCIETY

Secretary, Dr. H. W. Jacox, 4800 Friendship Ave., Meetings held second Wednesday each month, 4:30 P.M. October to June at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y. Secretary, Dr. S. C. Davidson, 277 Alexander St., Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

St. Louis Society of Radiologists

Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY

Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

<sup>\*</sup> Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

SOUTH CAROLINA X-RAY SOCIETY

Secretary, Dr. Hillyer Rudisill, Jr., Roper Hospital, Charleston. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

\*Tennessee Radiological Society

Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY

Secretary, Dr. H. C. Harrell, 517 Pine St., Texarkana, Texas.

University of Michigan Department of Roentgen-OLOGY STAFF MEETING

Meets each Monday evening from September to June. at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00-5:00 P.M., Room 301, Service Memorial Institute.

VIRGINIA RADIOLOGICAL SOCIETY

Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY

Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday of each month at the College Club, Seattle.

#### CUBA

SOCIEDAD CUBANA DE RADIOLOGIA Y FISIOTERAPIA Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

#### BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY

Meets monthly on third Thursday, from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London. Section of Radiology of the Royal Society of

MEDICINE (CONFINED TO MEDICAL MEMBERS) Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, I, Wimpole St., London, W. 1.

FACULTY OF RADIOLOGISTS

Secretary, Dr. Barbara M. Key, 32 Welbeck St., London, W.1, England.

Section of Radiology and Medical Electricity, Aus-TRALASIAN MEDICAL CONGRESS

Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

RADIOLOGICAL SECTION OF THE VICTORIAN BRANCH OF THE British Medical Association

Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussion. CANADIAN ASSOCIATION OF RADIOLOGISTS

Secretary, Dr. A. C. Singleton, Medical Arts Bldg., To-

ronto, 5, Ontario.

Section of Radiology, Canadian Medical Association Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S. RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL Association

Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

#### CONTINENTAL EUROPE

BELGIAN SOCIETY OF ROENTGENOLOGY

Secretary, Dr. J. Boine, Avenue des Ailiés, 134, Louvain (Belgium).

Meets monthly on second Sunday at d'Egmonds Palace. Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France

Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris. Société Suisse de Radiologie (Schweizerische Rönt-GEN-GESELLSCHAFT)

Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.

Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Société Franca se d'Electrothérapie et de Radiologie Médicale

Meets monthly on fourth Tuesday, except during month of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenglogists and Radi-OLOGISTS IN CZECHO-SLOVAKIA

Secretary, Dr. Walter Altschul, German University. Prague, 11.52.

DEUTSCHE RÖNTGEN-GESELLSCHAFT (GESELLSCHAFT FÜR Röntgenkunde und Strahlenforschung)

Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.

Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

SÜD- UND WESTDEUTSCHE RÖNTGENSELLSCHAFT

Meets annually in different cities.

NORD- UND OSTDEUTSCHE RÖNTGENGESELLSCHAFT

Meets annually in different cities.

DUTCH SOCIETY OF ELECTROLOGY AND ROENTGENOLOGY Holds two reetings a year in Amsterdam, one in the Spring, and me in the fall.

Societa Italiana Radiologia Medica Secretary, M. Ponzio, University of Turin, Prof. Turin Societatea Romana de Radiologie si Electrologie Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania.

Meets second Monday in every month with the ex-

ception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD, USSR in the State Institute of Roentgenology and Radiology, & Roentgen St.

Secretaries, Drs. S. A. Reinberg and S. G. Simonson.

Meets annually.

LENINGRAD ROENTGEN RAY SOCIETY

Secretaries Drs. S. G. Simonson and G. A. Gusterin. Meets moathly, first Monday at 8 o'clock State Institute of Reentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society

Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobeje sky. Meets monthly on first Monday at 8 o'clock.

POLISH SOCRETY OF RADIOLOGY

Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

WARSAW SECTION, POLISH SOCIETY OF RADIOLOGY Secretary, Dr. B. Krynski, 11 Zielna St. Meets once a month except in the summertime.

SCANDINAV AN ROENTGEN SOCIETIES

The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society or Medical Radiology in Sweden

Meets in Stockholm.

SOCIETY OF MEDICAL RADIOLOGY IN NORWAY • Meets in Oslo.

SOCIETY OF MEDICAL RADIOLOGY IN DENMARK Secretary, Dr. G. Biering, Copenhagen.

Meets the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

SOCIETY OF MEDICAL RADIOLOGY IN FINLAND

Meets a Helsingfors.

VIENNA LOENTGEN SOCIETY

Meets first Wednesday of each month, at 6:30 P.M. at Zentra-Röntgen Institut des allgemeinen Krankenhauses Alsersmasse 4.

#### ORIENT

JAPAN X-RAY ASSOCIATION

c/o Cathopedic Surgery, Tokyo Imperial University. Meets annually in April.

KINKI FOENTGEN-ABEND SOCIETY

Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

# REPORT OF THE RESEARCH AND STANDARDIZATION COMMITTEE OF THE AMERICAN RADIUM SOCIETY

HE effort made by this Committee in 1937 to collect information concerning methods used by members of the American Radium Society for treatments of carcinoma of the uterine cervix indicated a wide variation in methods both concerning the general plan of the treatments and the dose used. The progress in radium therapy has been considerable, but it is evident that no agreement has as yet been reached concerning the most efficacious method. Any attempt of this Committee to advocate certain types of treatments or to specify the dosage for any type of disease would therefore simply represent the opinions of its members.

The importance of the time distribution of the irradiation as particularly emphasized by Regaud and Coutard has been generally accepted. The complicated relations between the time factor and the biological effects are so difficult to determine that our knowledge in this field is still very limited in spite of many valuable investigations and observations. Though careful consideration of time distribution has led to improved results from treatments, it is impossible as yet to state accurately which time distribution would be the best one for treatment of a certain disease.

It is evident that the distribution of the radiation throughout the treated area must be carefully considered and that the determination of the total dose of radiation at different portions of the tissues as well as the rate of dose is of fundamental importance. Certain measurements and calculations have been made which are accurate enough to permit a general acceptance.

For the reasons given we have confined ourselves in this report to the consideration of the physical factors of radium and radon therapy. It seemed advisable to collect some data from publications during the last few years and arrange a set of reliable tables which would be useful for the mem-

bers of the Society. Between 1926 and 1930 the Society published the reports of the Research and Standardization Committee on loose leaves which could be assembled in folders. We wish to propose that this action be renewed. It seems, however, practical to make the loose leaves the same size as the Journal so that the same can be used both for publication in the Journal and the loose leaves. The old loose leaves were of smaller size, but they are now out of date, and the new tables are more accurate and complete and should therefore replace the old ones.

It would take too long a time to discuss the tables in detail, but some lantern slides will give an idea of the material. A few copies are available for those who desire to examine it in detail. We hope the Society will accept the full report for publication in the Journal and in a loose leaf form.

#### Physical Factors for Therapy with Radioactive Substances

When treatments are given with radium or radon, it is advisable to give the following factors:

- Amount of radium in milligrams or radon in millicuries.
- (2) The time of exposure in hours (days or minutes).

When radon implants are used and not removed, it is enough to give the number of millicuries per implant and the total number of implants as such a source always irradiates the same length of time. The total number of millicurie hours is 133 times the number of millicuries.

When the dose is split between several applications, the length of each treatment and the time interval between treatments should be given.

- (3) The kind and thickness of filter used.
- (4) The surface area over which the radium is spread.

If the individual applicators are placed some distance apart, the configuration should be described. If the irradiating



layer is more than I mm. thick (e.g. tubes placed on top of each other), the thickness should also be given.

- (5) The distance from the center of the applicator to the nearest point of the tissues (skin) should be accurately stated.
- (6) The three dimensions of the irradiated mass.
  - This information is of special importance when interstitial irradiation is used.
- (7) The approximate distribution of the sources within the tissues should also be outlined.

These factors give information which can be used for the calculation of the dose at the surface as well as at certain depths. The dose received by a small volume of tissue can be given in threshold erythema doses. It is, perhaps, more convenient to

Table I\*

RELATIVE AMOUNTS OF RADIATION TRANSMITTED
BY VARIOUS FILTERS†

M	Thick-	Amount of Radiation	Compo Rad	sition of iation
Metal	ness mm.	Relative to 0.5 mm. Pt	Beta (per cent)	Gamma (per cent)
Brass	0.5	160	33	67
	1.0	111	8	92
	2.0	100	0	100
	3.0	95	0	100
	4.0	92	0	100
Silver	0.5	128	17	83
	1.0	103	0	100
	2.0	94	0	100
	3.0	90	0	100
Lead	0.5	118	12	88
	1.0	97	0	100
	2.0	88	0	100
	3.0	83	0	100
Gold or	0.2	135	22	78
platinum	0.3	111	9	91
	0.5	100	0	100
	0.1	• 88	0	100
	1.5	82	0	100
	2.0	78	0	100
	3.0	73	0	100

<sup>\*</sup> From Quimby.9

TABLE II
(Calculated from Table 1)

CORRECTION FACTOR FOR ADDITIONAL FILTRATION
ABOVE 0.5 MM. PT

Additional Thickness of Metal	Brass Steel Monel	Silver Lead	Gold Platinum
0.5	1.03	1.05	1.14
0.1	1.05	1.10	1.22
1.5	1.07	1.13	1.28
2.0	1.09	1.16	1.33
2.5			1.37

express this dose in a concise physical unit. The roentgen has been used for this purpose and is adopted in the following tables. It must be kept in mind that this unit as here defined may not cause the same effect as I r of roentgen rays, and the  $\gamma$ -ray r is, therefore, specified as  $r_{\gamma}$ . A number of careful measurements carried out at different laboratories indicate that the following value is fairly accurate and the best obtainable at the present time.

A point source of 1 mg. of radium filtered with 0.5 mm. of platinum gives a dose of 8.3  $r_{\gamma}$  in one hour at a distance of 1 cm. If this value is accepted, it can be stated that 1,000  $r_{\gamma}$  given in less than two hours approximately corresponds to a threshold erythema dose.

#### A. Filters.

- 1. When  $\beta$ -rays are used for treatments the filtration must be light. Small variations in the material may influence the dose considerably. No satisfactory standards have been worked out. It is best to determine empirically suitable dosage for each applicator used. The dose falls off rapidly in the tissues and as an approximation it may be assumed that 75 per cent of the  $\beta$ -rays are absorbed by the first 2 mm. of tissue and 15 per cent in the next 2 mm.
- 2. As a simple rule it may be stated that the primary  $\beta$ -rays are removed by
  - 2 mm. of brass, copper, steel or monel metal
  - 1 mm. of lead or silver
  - 0.5 of platimum or pure gold.

<sup>†</sup> Metal filter only; no secondary filter used.

#### TABLE III

#### (The values of this table have been calculated)

Number of  $\gamma$ -ray roentgens in center of field obtained with 1 mg. in one hour at various distances from various flat applicators .

		100000	/	Radium	Evenly Di	stributed				
Distance cm.	Tu	bes	9,999,999 m., marene marene marene marene de marten de la 1862 (1962 m) en 1882 m	Circles						
		ngth n.		Diameter cm.						
	O	I	2	4	1	2	4	6	8	
0.5 1.0 2.0 3.0 5.0	33.2 8.3 2.07 0.923 0.332	25.I 7.7 2.03 0.908 0.330	18.3 6.55 1.92 0.888 0.327	11.0 4.51 1.63 0.815 0.316	23.0 7.4 2.02 0.916 0.332	13.4 5.75 1.85 0.873 0.325	5.87 3·34 1.43 0.763 0.307	3·33 2·12 1·09 0·639 0·283	2.16 1.47 0.835 0.534 0.257	

#### Radium Placed at the Periphery Only

WHEN THE DIAMETER OF APPLICATOR IS LARGER THAN TWICE THE DISTANCE, THE MAXIMUM DOSE IS REACHED SOME DISTANCE FROM THE CENTER OF THE FIELD AND IS LARGER THAN THE FIGURES IN THE TABLE.

		1	Circles			The second secon		Squares			
Dis- tance	Diameter cm.					Length of sides cm.					
cm.	I	2	4	6	8	I	2	4	6	8	
0.5 1.0 2.0 3.0 5.0	16.60 6.64 1.95 0.90	6.64 4.15 1.66 0.83 0.32	1.95 1.66 1.05 0.64 0.29	.90 .83 .64 .46	.51 .49 .42 .33 .20	14.3 6.20 1.93 .89	5 · 43 3 · 65 1 · 55 · 80 · 32	1.55 1.35 .907 .585 .274	.710 .670 .531 .401 .225	.404 .389 .340 .280	

#### Rectangles

Distance cm.	$_{ m I}  imes _{ m 2}$	2×4	4×6	6×8
• .5 1.0 2.0 3.0 5.0	9.9 4.9 1.74 .85	3.98 2.50 1.23 .69	1.13 1.01 .719 .493 .250	.557 .485 .436 .340 .203

Table I gives the relative amounts of radiation transmitted by various filters.

3. Gamma rays produce secondary  $\beta$ rays in the filter. The intensity of these
rays is a minimum in substances of intermediate atomic number. It therefore

should be an advantage to have the outside wall of the container which comes in contact with the tissues made of brass, copper, monel metal, steel or nickel. If a small diameter is essential containers made of platinum or pure gold with a 0.5 mm. thick



wall are best. These can be placed inside capsules made from one of the other metals mentioned if space is available. The increased distance between the radium and the tissues contributes to protection of the surface and to an increased relative depth dose. The  $\gamma$ -ray intensity is reduced as the filter is increased. Thus, it takes 37 per cent longer time to give the same dose with radium filtered through 3 mm. of platinum than with the same amount of radium filtered through 0.5 mm. of platinum (Table II). The increase in penetration of the radiation in tissues is very small when the filter is increased from 0.5 to 3.0 mm. of platinum.

The number of milligram-hours (or the time) calculated for 0.5 mm. Pt filter should be multiplied by the factor found in this table in order to obtain the same dose when the corresponding filter has been added.

#### B. Surface Dose.

The dose at the surface obtained with 1 mg. of radium in one hour depends upon the distance as well as upon the distribution of the radium. Table III gives the number of  $\gamma$ -ray roentgens obtained at the surface without back-scattering for different distances and different distribution of the radium.

#### C. Depth Dose.

The relative depth dose expressed in per

Table IV

PERCENTAGE DEPTH DOSES FOR RADIUM

APPLICATORS

Filter 0.5 mm. Pt

	A	rea of A	pplicato	r—sq. cı	n.				
Depth	2	5 •	20	5	0				
cm.	Radium-Skin Distance—cm.								
	I	2	3	6	10				
0	100	100	100	100	100				
0.5	44	68	77	85	89				
I	28	52	62	75	81				
2	13	30	43	62	- 69				
3	4	20	31	51	59				
5		9	19	36	44				
7			12	25	33				
10			4	20	25				

#### TABLE V

RELATIVE INTENS TIES OF RADIATION FROM INTRA-CAVITARY APPLICATORS OF DIFFERENT DIAMETERS, IN FIRST CENTIMETER OF GISSUE

Filter 0.5 mm. Pt and 0.5 mm. Monel (This table is for needles 4 cm. long. For other lengths the values would be different)

Distance from	n Outside Diameter—mm.						
Surface mm.		5.0 Intensity of					
0	100	100	100				
1	57	66	74				
3	28	39	46				
5	17	25	33				
7	12	20	27				
10	9	14	20				

<sup>\*</sup> From Sievert.18

cent of the surface dose is given for a few applicators, based upon measurements made by Oumby and Failla.\* The distance from applicator to surface is short. The errors incroduced because of the size and shape of the ionization chamber, etc., may therefore be considerable, and the accuracy is not as great as in depth dose charts for roentgen rays where the distances are larger. The filter used for the measurements was equivalent to 0.5 mm. platinum. It is evident that the values can be used for heavier filters also as the depth dose does not increase to an appreciable extent when the filter is ir creased up to 3 mm. of platinum. Table IV refers to applicators with the radium evenly distributed over the surface. Under the same conditions but with the radium placed only at the periphery, a greater number of milligram-hours should be required to produce the same skin reaction and the depth dose should be greater than the values in the table.

When radium tubes are used in cavities, the dose in the tissue falls off rapidly at increasing distances from the applicator. It is then necessary to give a large dose to the surface ir order to apply an appreciable dose at 1 cm. depth. It is evident that the

<sup>\*</sup> Chapter on Rædium Dosimetry. The Science of Radiology. Edited by O. Glasser. Charles C. Thomas, Springfield, Illinois, 1022

TABLE VI (Calculated)

MG-HR, OR MC-HR, NECESSARY TO DELIVER 1 T.E.D.  $(1,000~r_{\gamma})~\text{AC}~\text{Different distances from}\\ \text{SOURCES OF VARIOUS LENGTHS}$ 

Filter-0.5 mm, Pt

		Acti	ve Length	-cm.	
Distance* cm.	0.5	1.0 mg- or	2.0 mc-hr. for	4.0 T.E.D.	6.0
0.5	35	45	60	100	140
1.0	135	150	180	250	340
2.0	540	570	600	700	780
3.0	1160	1180	1225	1350	1500

<sup>\*</sup> The distance is measured along a line perpendicular to the source at its center.

same dose at 1 cm. depth can be obtained with a relatively smaller surface dose if the tube is placed in a capsule of suitable light material so that the diameter of the applicator is increased. Table V gives the relative

dose in the tissues at 0 to 10 mm. distance from the surface of applicators of different diameters. If the same dose were applied at 1 cm. depth with such applicators the dose in the first millimeter of tissue would be about twice as large with the applicator 3 mm. thick as with the applicator 7 mm. thick.

The number of milligram- or millicuriehours required to deliver 1,000  $r_{\gamma}$  to different distances from 0.5 mm. platinum needles placed in tissues is given in the following table for needles of various active lengths.

Quantities of Radiation Necessary to Deliver Specified Minimum Doses in Various Tissue Volumes

In Table VI it can be seen that 1,000  $r_{\gamma}$  is obtained in the tissues at 1 cm. distance from a 5 mm. long needle with 0.5 mm.

Table VII\*

QUANTITIES OF RADIATION NECESSARY TO DELIVER SPECIFIED MINIMUM

DOSES IN VARIOUS TISSUE VOLUMES

•		Inters	titial Sou	rces				Filter 0.3	-0.5 mm	. Pt	
				Diamo	eter of Sp	herical N	lass—cm.		A Section of Contrast of Contr	Andrew Co. Co. and Co.	
	1	1.5	2.0	2.5	3.0	3 · 5	4.0	4 · 5	5.0	5 - 5	6.0
MA AND TO ME AND AND	·	, aportone gradula, distance la	and the constitution of the second of the second	Volume	of Mass-	-Cubic (	Centimete	rs		Annual Control of the	han-Thomas - consumptible results
	0.5	2	4	8	15	25	35	50	65	90	115
T.E.D.			Mill	igram- or	Millicur	ie-Hours	to Delive	r Specifie	d Dose		
I	35	80	135	250	330	420	540	680	830	1000	1160
2	70	160	270	500	660	840	1080	1360	1660	2000	2320
3	105	240	405	750	990	1260	162c	2040	2490	3000	3480
4	140	320	540	1000	1320	1680	2160	2720	3320	4000	4640
5	175	400	675	1250	1650	2100	2700	3400	4150	5000	5800
7	245	560	945	1750	2310	2940	3780	4760	5810	7000	8120
10	350	800	1350	2500	3300	4200	5400	6800	8300	10,000	11,600
belts whether the transfer about the orbits of the second the orbits of the second the second the second the second terms of t	uh barhasin 1996, dibandan da Milli (Milli (Milli (Milli)))	and the second s	Mill	icuries-D	estroyed	to Delive	er Specifie	d Dose			
1	0.25	0.6	0.1	1.9	2.5	3.2	4.0	5.0	6.2	7 - 5	8.7
2	0.5	1.2	2,0	3.8	5.0	6.4	8.0	10.0	12.0	15.0	17.0
3	0.75	1.8	3.0	5 - 7	7 - 5	9.6	12.0	15.0	18.0	22.0	26.c
4	0.1	2.4	4.0	7.6	10.0	13.0	16.0	20.0	25.0	30.0	35.0
5	1.25	3.0	5.0	9 - 5	12.0	16.0	20.0	25.0	31.0	38.0	44.0
7	1.75	4.2	7.0	13.0	0.81	23.0	28.0	35.0	43.0	52.0	61.0
10	2.50	6.0	10.0	19.0	25.0	32.0	40.0	50.0	62.0	75.0	87.0

<sup>\*</sup> Syllabus of Lectures—The Physical Basis of Radiation Therapy. Edith H. Quimby, Memorial Hospital, New York City, 1939.



Table VIII\*

DECAY OF RADON AND ENERGY EMITTED DURING DECAY

Tir	me	. Per Cent Remaining	Mc-hr. per Initial mc.	Т	ime	Per Cent <sup>•</sup> Remaining	Mc-hr. pe Initial mc
Days	Hours	THE MATERIAL PROPERTY OF THE PROPERTY OF T		Days	Hours		
0	0	100	0	2	20=	59.82	53.42
	2	98.50	1.99	3	O:	58.05	55.80
	4	97.02	3.96	3	6	55.47	59.26
	6	96.67	5.90	3 3	1.2	53.01	62.44
	8	94.14	7.82	3	18-	50.71	65.60
0	10	92.72	9.62	4	a	48.42	68.60
	12	91.33	11.52	4	8	45.60	72.41
	14	89.98	13.33	4	16	43.57	75.07
	16	88.61	15.11	5	G.	40.43	79.30
	18	87.28	16.96	5	8	38.02	82.52
0	20	85.98	18.64	5	16	35.78	85.40
	22	84.96	20.38	6	C	33.70	88.40
1	0	83.42	22.08	6	12	30.80	92.15
1	3 6	81.55	24.55	7	C	28.11	95.78
1	6	79.72	26.97	7	12	25.67	99.00
I	9	77.93	29.35	8	C.	23.45	102.1
1	12	76.18	31.70	9	C-	19.56	107.0
1	15	74.48	33.98	10	C	16.32	111.4
1	18	72.81	36.16	11	C	13.61	118.0•
I	21	71.18	38.38	12	C	11.35	0.811
2	0	69.59	40.45	14	C	7.90	122.5
2	4	67.52	43.20	17	¢	4.59	125.8
2	8	65.50	45.91	20	€-	2.66	129.4
2	12	63.55	48.51	25	4	1.07	131.5
2	16	61.66	51.00	30	€ë÷	0.43	132.5

<sup>\*</sup> International Radium Standards Commission. J. Am. Chem. Soc., 1931, 53, 2437-2451.

platinum wall if 135 mg-hr. are used. It is therefore evident that the periphery of a spherical mass of tissue 2 cm. in diameter receives approximately 1,000 r<sub>y</sub> if such a small needle is placed in the center and permitted to deliver 135 mg-hr. of radiation. If the radium could instead be distributed evenly at the periphery of the sphere of 2 cm. diameter, it is evident that the same number of milligram-hours would deliver about 1,000 r, to the center. In either case 1,000  $r_{\gamma}$  is the minimum dose delivered to any part of a spherical mass. The latter distribution of the radium would give a more homogeneous dose. This distribution can be approached by using a

number of small applicators placed symmetrically at the periphery of the mass. From a practical point of view the sources cannot be distributed evenly over the periphery, and somewhat greater variation in dosage therefore has to be expected. Tables have been made to show how many milligram-hours are needed to deliver 1,000  $r_{\gamma}$  to any size spherical mass. Such tables which are partly checked by actual experiments show that the "inverse square law" gives values which are accurate enough for masses up to 6 cm. diameter. If the diameter is 1 cm, 34 mg-hr. are needed to deliver 1,000 r, and the square of the diameter in centimeters times 34 gives the number

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of milligram-hours required to deliver a minimum dose of 1,000  $r_{\gamma}$  to any particular sphere. The number of millicuries-destroyed to deliver 1,000  $r_{\gamma}$  is equal to 0.25 times the square of the diameter in centimeters. Masses of other shapes may be considered as several spheres.

Radon implants are often used for interstitial irradiation. If gold implants are used with 0.3 mm. thick wall the dose in  $\gamma$ -ray roentgens would be slightly larger than for the 0.5 mm. platinum filtration.

The effect on the tissues depends also upon the time distribution of the radiation; 1,000  $r_{\gamma}$  corresponds to a threshold erythema dose when given in a relatively short time. Table VII gives the relation between milligram-hours or millicuries-destroyed and threshold erythema dose.

As a matter of fact no considerations of time effect have been used in developing this table. It is a strictly physical equality.

A minimum dose of 7,000 r<sub>7</sub> is often required for treatments of carcinoma. When large tumors are treated, it is necessary to consider the general effects of the radiation, and it is not always possible to give the full dose required in one application. This table is for sources of radiation distributed uniformly throughout the mass.

When radon is used for treatments, the disintegration of this element has to be accurately considered. Table VIII gives the percentage of radon remaining after various time intervals. If the "strength" of a radon container is known at a certain time, its strength at any other time can therefore be calculated by means of these values.

Table IX

TIMES REQUIRED TO DELIVER CERTAIN MILLICURIE-HOUR PER INITIAL MILLICURIE

Mc-hr. per	th immediate and	Time	- Property and the second	Mc-hr. per	T	ime
Initial mc.	Days	Hours	Minutes	Initial mc.	Days	Hour
2	0	2	I	52	2	2
4 6		4	4	54	2	21
		6	9	56	3	1
8		8	16	58	3	4
10		10	25	60	3	<b>4</b> 7
12		12	36	62	3	11
14		14	50	64	3	15
16		17	13	66	3	19
18		19	24	68	3	23
20		21	44	70	4	3
22	I	0	6	72	4	7
24	I	2	32	74	4	11
26	1	5	0	76	4	16
<ul><li>28</li></ul>	I	7	30	78	4	21
30	1	10	5	78 80	5	2
32	1	12	42	82	5	7
34	I	15	14	84	5	12
36	I	18	4	86	5 5 5 6	17
38	I	20	51	88	5	23
40	1	23	42	90	6	5
42	2	2	42	95	6	21
44	2	6	9	100	7	16
46	2	8	4	IIO	9	17
48	2	11	14	120	12	20
50	2	14	20	130	21	0

The table also gives the number of millicurie-hours of radiation obtained from 1 mc. in a certain length of time.

It is important to know for how long a time a certain amount of radon should be used to deliver an even number of millicurie-hours. Table IX can be used for this purpose. If the number of millicurie-hours desired is divided by the number of millicuries available at the beginning of the treatment, the number of millicurie-hours per initial millicurie which is required is found. By looking up this figure in column one, the corresponding time is found in the next columns. (Interpolate if necessary.)

Further information concerning physical measurements can be found in the radio-logical journals. The following publications have been used as a basis for this report:

- 1. Science of Radiology. Edited by Otto Glasser. Charles C Thomas, Springfield, Illinois, 1933.
- 2. Failla, G. Development of filtered radon implants. Am. J. Roentgenol. & Rad. Therapy, 1926, 16, 507-525.
- 3. Recommendations of the International Committee for Radiological Units (Chicago, 1937). Radiology, 1937, 29, 634-636.
- 4. LAURENCE, C. G. Radium Dosage. National Research Council of Canada, Bulletin No. 17, 1936.
- MARTIN, H. E., QUIMBY, E. H., and PACK, G. T. Calculations of tissue dosage in radiation therapy. Am. J. ROENTGENOL. & RAD. THER-APY, 1931, 25, 490-506.
- 6. Mayneord, W. V. Distribution of radiation around simple radioactive sources. *Brit. J. Radiol.*, 1932, 5, 677-716.
- 7. PATERSON, R., and PARKER, H. M. Dosage system for gamma ray therapy. Brit. J. Radiol., 1934, 7, 592-632.
- 8. Paterson, R., and Parker, H. M. Dosage system for interstitial radium therapy. Brit. J. Radiol., 1938, 11, 252; 313.
- QUIMBY, EDITH H. Comparison of different metallic filters used in radium therapy. Am. J. ROENTGENOL. & RAD. THERAPY, 1925, 13, 330-342.
- 10. QUIMBY, EDITH H. Effect of the size of radium applicators on skin doses. Am. J. ROENT-GENOL. & RAD. THERAPY, 1922, 9, 671-683.
- 11. QUIMBY, EDITH H. Intensity of radiation in the vicinity of filtered radon implants. *Radiology*, 1928, 10, 365–376.
- 12. QUIMBY, EDITH H. Physical factors in interstitial radium therapy. Am. J. ROENTGENOL. & RAD. THERAPY, 1935, 33, 306-316.

- SIEVERT, R. M. Die γ-Strahlungsintensität an der Oberfläche und in der nächsten Umgebung von Radiumnadeln. Acta radiol., 1930, 11, 249-301.
- 14. Stenstrom, W. Physical factors in teleradium therapy. Am. J. Roentgenol. & Rad. Therapy, 1935, 33, 296-301.

Submitted by the Research and Standardization Committee at the Annual Meeting of the American Radium Society at St. Louis, May 15, 1939.

WILHELM STENSTROM, Ph.D. EDITH H. QUIMBY, M.A. EUGENE P. PENDERGRASS, M.D.

### MINNESOTA RADIOLOGICAL SOCIETY

The Fall Meeting of the Minnesota Radiological Society was held at the Mayo Clinic, Rochester, Minnesota, in the afternoon of December 2, 1939. The following program was given:

Experiences with roentgen pelvimetry. G. A. Good, M.D., and A. B. Hunt, M.D.

The proctosigmoiditis of lymphogranuloma venereum. H. M. Weber, M.D.

Pseudo fractures in diseases affecting the skeletal system. Discussion by J. A. L. Mc-Cullough, M.D., and J. D. Camp, M.D.

The evaluation of prostigmine, barium chloride, oxygen and pitressin for the elimination of flatus, in roentgenograms of the abdomen. E. E. Seedorf, M.D.

Primary carcinoma of the lung:

Roentgen diagnosis. J. W. Ölds, M.D. Roentgen treatment. E. H. Little, M.D. Discussion. E. T. Leddy, M.D.

Intrathoracic tumors, S. W. Harrington, M.D.

A business meeting was held after the program, followed by a dinner at 6.30 p.m. at the Hotel Kahler. The speakers at the dinner were H. M. Worth, M.D., who discussed "Radiology in England" and Shaohsun Wang, M.D., whose topic was "The Practice of Medicine in China."

#### CONFERENCE OF MID-WESTERN RADIOLOGISTS

The Fourth Annual Clinical Conference of Mid-Western Radiologists will be held at the Brown Hotel, Louisville, Kentucky, on February 9 and 10, 1940. In the program emphasis is placed on the clinical aspects of problems of interest to radiologists. Most of the presentations are to be given by physicians active in the practice of clinical medicine. The Kentucky Radiological Society is host to the Conference.

J. C. Bell General Chairman

#### CORRECTION

In the article by E. A. Merritt on

"Roentgen Therapy of Cancer in the Buccal Cavity and of the Cervix Uteri" in the September, 1939, issue of the JOURNAL, the following corrections should be noted:

The first sentence, page 418, should read "Radium therapy in carcinoma of the cervix uteri is almost universally recognized and accepted."

Under Summary, page 420, the first line of the third paragraph should read "Infection is controlled so that, with 1 per cent bicarbonate soda douches during treatment"....







#### DEPARTMENT OF TECHNIQUE

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# ROENTGEN MEASUREMENT OF THE OBSTETRICAL CONJUGATE OF THE PELVIC INLET

By PAUL C. HODGES, Ph.D., M.D., JANE E. HAMILTON, M.S., and JED W. PEARSON, JR., M.D.

From the Division of Roentgenology, and the Department of Obstetrics, University of Chicago CHICAGO, ILLINOIS

THE importance of the roentgen measurement of the obstetrical conjugate of the pelvic inlet is now thoroughly established in obstetrics and roentgenology. Most workers use lateral roentgenograms, the methods employed for correcting for triangular distortion falling under three general heads:

1. Correction by Means of a Sacral or Pubic Marker. A calibrated metal scale is supported above the film and parallel with it at a level supposed to be identical with the level of the sacral promontory and the pubic symphysis. Some workers place the marker in the gluteal cleft, others place it in front of the pubic symphysis. The scale may be notched or perforated at 1 or 0.5 cm. intervals, in which case no computations are needed, the calipered gross conjugate being laid off directly on the image of the marker which is used as a false centimeter scale. Instead of a calibrated marker one may use a marker with only two points on it, the distance between the two being known. Under these conditions correction of the gross conjugate is accomplished by multiplying it with a factor F obtained from the equation

$$F = \frac{M}{y}$$

where

M= the actual distance between the points on the marker

y=the distance between the image of these points as seen in the film.

2. Correction by Means of Sacral or Pubic Measurement. When target-film distance (D) and table-top-film distance (e) are fixed and known and the distance from the middle of the sacrum or the pubic symphysis to the top of the table (h) can be measured, no marker is needed, the correction factor being obtained from a graph

of the equation 
$$F = \frac{D - (h + e)}{D}$$
. It is pos-

sible to build roentgen apparatus in which D and e are fixed and known; h, however must be measured for each patient, and in our opinion if this measurement is to be significant it must be made by the roentgenologist himself at the time the film is exposed.

3. Correction by Means of Parallax. When suitable apparatus is available, accurate measurements of the obstetrical conjugate may be obtained by stereoscopic triangulation, the degree of accuracy depending almost solely upon the precision of the apparatus and the technique of the person who works up the films. We prefer to work up such films by direct measurement of parallax1 but one may use instead a stereoroentgenometer or a measuring stereoscope. The parallax methods are particularly adaptable to institutions where the volume of work is large and the actual film making is done by technicians. They have the disadvantages of requiring two films rather than one and of requiring considerable time

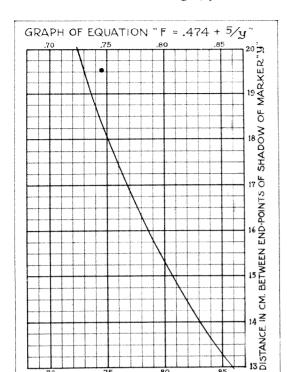


Fig. 1, Graph for obtaining triangular distortion correction factor from surface marker for correction of obstetrical conjugate as seen in lateral pelvic roentgenograms.

.70 .75 .80 .85 TRIANGULAR DISTORTION CORRECTION FACTOR

for the working up of the films after they have been made.

#### CORRECTION BY A SURFACE MARKER

The present paper deals with a one-film method for the measurement of the obstetrical conjugate, in which accuracy depends largely upon the precision of the apparatus. The technician must see to it that the patient is in the true lateral position and must bring the arm of a special marker down until it presses firmly against the skin over the uppermost great trochanter, but in our opinion capable technicians can be depended upon for these details. There are no measurements for the technician to make. The method assumes that the conjugate lies halfway between the two great trochanters but the validity of the measurement is affected surprisingly little by pelvic asymmetry even of considerable degree.

The marker is an aluminum arm carrying two perforated lead discs, the perforations being 10 cm. apart. This arm can be moved up or down along a rod that rises perpendicular to the plane of the table top. The perpendicular rod may be supported by a weighted base resting on the table top or it may be attached to a fitting that slides along a rail for the attachment of other accessories. The subject is placed in the lateral position on the roentgen table, her legs flexed on the thighs, her thighs extended on the pelvis as far as comfort will permit. This position increases the lordosis of the spine, brings the anteroposterior diameter of the pelvic inlet more nearly parallel with the long axis of the film and prevents the shadows of the thighs from obscuring those of the pelvis. Either lateral view is satisfactory but with our own apparatus it is more convenient to have the patient lying left side down and the following description refers to the left lateral position.

A single 10"×12" film is lined up so that its center lies approximately on an imaginary perpendicular axis passing from the target of the roentgen tube down through a point midway between the perforations on the marker and a point midway between the sacral promontory and the pubic symphysis. Accuracy in this alignment of tube, marker, subject and sacrum facilitates identification of the end-points of the conjugate but does not otherwise affect the accuracy of the measurement. As long as these end-points and the perforations in the marker can be seen the film is suitable for measurement.

The general equation for the correction factor is

$$F = \frac{D - e}{2D} + \frac{M}{2y}$$

where

F=correction factor for obtaining net or true conjugate from the gross or distorted conjugate measured on the film

D = target-film distance (in our apparatus 88.5 cm.)

#### DERIVATION OF EQUATION

Equation

Explanation

1. 
$$\frac{a}{D-h} = \frac{I}{D}$$

Triangular proportion based on Figure 2.

$$2. \quad a = I\left(\frac{D-h}{D}\right)$$

No. 1 simplified.

3. 
$$a = IF$$

From No. 2  $\frac{D-h}{D}$  is a factor F which multiplied by the image

$$4. \frac{f}{g} = n \quad f = ng$$

of the conjugate I yields the true diameter of the conjugate a. In most cases n=1 but the method is correct within experimen-

5. 
$$d=h+f$$

See Figure 2.

6. 
$$d=h+ng$$

Substituting in No. 5 the value of f from No. 4.

tal limits over a considerable range of values of n.

7. 
$$g = h - e$$

See Figure 2.

8. 
$$d=h+nh-ne$$

Substituting in No. 6 the value of g from No. 7.

$$9. \quad h = \frac{d + ne}{n + 1}$$

No. 8 simplified.

$$10. \quad h = \frac{d+e}{2}$$

In symmetrical pelves where n=1.

11. 
$$\frac{M}{D-d} = \frac{y}{D}$$

Triangular proportion based on Figure 2.

$$12. \quad d = \frac{D(y - M)}{y}$$

No. 11 simplified.

13. 
$$F = \frac{D - h}{D}$$

From Equation No. 3.

$$D - \left(\frac{d+e}{2}\right)$$
14.  $F = \frac{D}{D}$ 

Substituting in No. 13 the value of h from No. 10.

$$D - \left[ \frac{D(y-M)}{y} + e \right]$$
15. 
$$F = \frac{D}{D}$$

Substituting in No. 14 the value of D from No. 12.

16. 
$$F = \frac{D - e}{2D} + \frac{M}{2v}$$

No. 15 simplified.

17. 
$$F = .474 + \frac{5}{y}$$

Substituting in No. 16 the values for D, e and M in our particular apparatus.

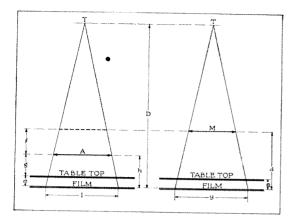


Fig. 2. D, target-film distance; e, table-top-film distance; A, actual distance between sacral promontory and pubic symphysis (obstetrical conjugate): I, gross or distorted image of obstetrical conjugate as seen in roentgenograms; h, height of sacrum and pubic symphysis above plane of film; f, distance from sacral promontory and pubic symphysis to skin above right great trochanter (patient lying in left lateral position); g, distance from sacral promontory and pubic symphysis to skin above left great trochanter; M, distance between the points on a surface marker placed in contact with the skin over the right great trochanter and arranged parallel with the plane of the film; y, distance between points on the distorted image of the marker as seen in the roentgenogram; d, the height of the marker above the film; D, e and Mare fixed and known. I and y can be measured on the film.

e = distance between the upper surface of the table top and the plane of the film (in our apparatus 4.6 cm.)

M=actual distance between the points on the marker (in our apparatus 10 cm.)

y = gross distance between the shadows of these points as seen in the film Substituting these values, the equation for our own particular apparatus becomes F = 0.474 + 5/y. For convenient application this equation is expressed as a graph (Fig. 1).

This method is the direct outgrowth of a procedure developed by us for the measurement of occipitofrontal diameter in fetal skulls. We have published skull measurements obtained in this manner<sup>2</sup> but have not heretofore described the method of making the measurements.

#### EXPERIMENTS

Ten subjects were examined, three films being made in each case—a stereoscopic pair for parallax and one with the tube directly above the center of the film for the position methods. In 9 of the cases computations were made by parallax, by means of the sacral marker, by sacral measurement and by means of the surface marker.

TABLE I

	Parallax	Obstetrical Conjugate in Centimeters Measured by								
Case No. used as Standard	Sacral Marker	Error	Sacral Measure- ment	Error	Surface Marker	Error				
I •	12.1			A 1 A 1999 to a resolution to the second contract of the second cont		11.9	2			
2	12.1	12.7	+.6	12.3	+.2	12.2	+.1			
3	11.4	11.8	+.4	11.4	.0	11.5	+.1			
4	10.9	11.3	+ 4	11.2	+.3	10.9	.0			
5	9.9	10.2	+.3	10.0	+.1	9.8	1			
6	11.3	11.5	+.2	11.1	2	11.3	.0			
7	13.9	13.8	1	14.3	+.4	13.6	3			
8	11.5	11.8	+.3	11.5	.0	11.5	.0			
9	12.3	12.6	+.3	12.4	+.1	12.2	I			
10	12.3	12.8	+.5	12.3	.0	12.1	2			
Average			+.3		+.1	OFFICE AND ADMINISTRATION OF THE PROPERTY OF T	07			

In one case, only parallax and sacral marker measurements were obtained. Assuming, for the sake of argument, that the parallax measurements are an accurate indication of the actual measurement of the obstetrical conjugate, it was found that with the surface marker there was a mean error of -0.7 mm., with the sacral measurement a mean error of +1 mm., with the sacral marker a mean error of +3 mm. The details are given in Table 1.

#### CONCLUSIONS

1. There is presented an objective method for the measurement of the obstetrical conjugate of the pelvic inlet by means of a single lateral pelvic roentgenogram.

72. The only special apparatus needed is a 10 cm. scale that rests on the uppermost great trochanter supported so that it lies parallel with the plane of the film.

3. Net or true obstetrical conjugate is computed by measuring the conjugate as it appears on the film and multiplying this gross value by a factor F obtained from the equation

$$F = \frac{D - e}{2D} + \frac{M}{2y}$$

where

F = correction factor

D = target-film distance

e = table-top-film distance

M = diameter of the surface marker

y = diameter of the roentgen image of

#### REFERENCES

the surface marker.

- I. Hodges, P. C. Roentgen pelvimetry and fetometry. Am. J. Roentgenol. & Rad. Therapy, 1937, 37, 6-4-662.
- 2. Hodges, P. C., and Hamilton, J. E. Pelvic roentgenography in pregnancy. *Radiology*, 1938, 30, 157-166.



## A SIMPLE TECHNIQUE AND NEW INSTRUMENT FOR RAPID ROENTGEN PELVIMETRY\*

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 NEW YORK CITY

#### I. INTRODUCTION

A<sup>S</sup> roentgen pelvimetry becomes more generally used, there is increasing need for a simple, coherent technique. At present there is an understandable skepticism about pelvimetry on the part of some obstetricians who have delivered babies per vaginam after a roentgenologist has given the opinion that they could not be so delivered. Obviously they could, and were. But should they have been? Many a family may be bearing the stigma of mental insufficiency in a child through no fault of its genes, but because of cerebral trauma at birth. In considering this problem, due recognition is given the fact that soft tissue architecture and pelvic dynamics are factors in its solution.

The requirements for a reliable system of pelvimetry, which this paper is designed to construct, are these:

- 1. Simplicity. The method demands nothing beyond ordinary roentgen-ray facilities, not even stereoscopy. Two roentgen exposures of the pelvis, a centimeter rule, and a chart or instrument for distortion correcting are all that is necessary. Reading the directions is, naturally, far more time consuming than actually making the computations.
- 2. Intelligibility. These measurements are not to be made by engineers, but by obstetricians and roentgenologists. The fundamental concepts are certainly comprehensible to any physician who is willing to read the explanation.
- 3. The accuracy of the measurements can usually be considered not more than 0.5 cm. out of the way.
- 4. The reports are in linear distances, the same as those with which the obstetrician has been familiar for years. The following measurements are computed:

#### Pelvic Inlet:

- True conjugate or anteroposterior diameter.
- 2. Widest transverse diameter. *Mid-pelvis:*
- 1. Bisischial, or transverse diameter at ischial spines.
- 2. Anteroposterior diameter from hollow of sacrum to a line even with the symphysis.

Pelvic Outlet:

- 1. Tuberischial, transverse diameter.
- 2. Posterior sagittal, anteroposterior from lower sacrum to middle of tuberischial line.

Fetus:

1. Circumference of skull, from which can be recognized the size of the fetus as well as its age in weeks.

The method to be presented requires not more than a few minutes for completing an entire set of measurements and calculations. It is amply accurate for clinical use.

#### II. FUNDAMENTAL CONCEPTS

A man's shadow, as he walks along the street, may measure several feet larger than he, and the roentgen shadow of a pelvic bone, likewise, is somewhat larger than the bone itself.

How much larger is a given true conjugate on the film, over the real, anatomic distance? It is self evident that if the roentgen tube is kept at the same distance (and it always must be at just 30 inches from the film with the method to be described), the disproportion between real size and size on the film will depend on the distance of the pelvis from the film. The closer the pelvis approaches to the film, the less will be the exaggeration of its size. Mathematically speaking, with similar

<sup>\*</sup> From the Harlem and Bronx Hospitals, New York City.

triangles the bases are proportional to the altitudes, or:

#### tube-film distance

tube-film distance minus object-film distance

> image diameter object diameter

The problem, then, is: How far was the pelvis, or that portion of it under consideration, from the film when the roentgenogram was taken? Assume it is the true conjugate we are measuring, and we are looking, therefore, at the lateral view. The patient was lying on her right side when this exposure was made: that is, the true conjugate was separated from the table by the distance from the trochanter (on which she was lying) to the symphysis. But what is this distance between trochanter and symphysis? That can be directly measured on the other film, which was taken as an anteroposterior view.

The acquired data now are:

- (a) Measured distance between promontory and symphysis—on the lateral view.
- (b) Distance of this diameter (true conjugate) from the film—on the anteroposterior view.

Simple geometry as was stated yields, finally, the desired measurement: the true, anatomical diameter.

In brief, we measure a diameter on one film and determine from the other film just how far from the table that diameter lay. With these two measurements and the known tube-film distance, we can solve for the anatomical distance.

The second measurement (the objectfilm distance) is called the "correction factor." The interposition of the soft tissues between the bony parts and the table has been taken into account in arriving at an accurate correction factor. It will be quickly recognized, furthermore, that the correction factor is not critical a difference of centimeters in the correction

factor represents a difference in the final answer of only millimeters.

#### III. EQUIPMENT

The State-Rule. In the familiar proportion formula, we could substitute the three known quantities and solve for the anatomic distance. But this would be a tiresome procedure, and one subject to arithmetic errors. There are available several short-cut methods for computing this equation. Since these methods were not as rapid and as simple as could be desired, we fashioned a simplified slide-rule, designed especially for this system of pelvimetry. Its use is self explanatory and very easy see Fig. 3).

If the sade-rule is not used: Since the film, when exposed through a Potter-Bucky daphragm, is 5 cm. below the table top, this 5 cm. must be added to the "correct on factor" (the object-film distance). The roentgenogram, after all, shows object-to-table-top distance; but we must know object-to-film distance. (This 5 cm. is neelected when using the slide-rule, since it was added in the design of the instrument.)

The Twirled Adhesive. Measuring the circumference of the fetal skull, as described later, presented mechanical difficulties. We have found it convenient to use the following: A 50 cm. length of ordinary adhesive tape, I cm. wide, is rolled with its gammed side out—making a long, thin tube with considerable "stickiness." This can be placed along the skull edge, with the film on the shadow-box, and a crease made to designate the length of the circumserence. The adhesive tape is then measured on any centimeter scale.

Crayan. It is advantageous to mark significant points before measuring. "Chinamarking" and "eyebrow" pencils are very good. These marks can later be erased without damage to the film.

The Films. The two films consist of a lateral and an anteroposterior view of the pelvis. They must include symphysis, sacrum, tuberosities and trochanters. They are taken with the target just 30 inches (76 cm.) from the film, using a Potter-Bucky diaphragm. Two hundred cubic centimeters of air in the bladder help in locating the posterior margin of the symphysis (and incidentally, this provides contrast for soft tissue observations). In

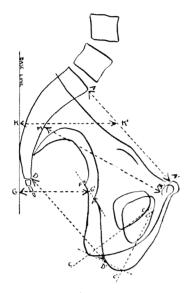


Fig. a. Lateral view of pelvis for locating measurements described in text. AA<sup>1</sup>, anteroposterior diameter of pelvic inlet; cc and c<sup>1</sup>c<sup>1</sup>, guide lines for locating tuberischial points; DD<sup>1</sup>, posterior sagittal diameter of pelvic outlet; FF<sup>1</sup>, location of spines on lateral view of pelvis; GG<sup>1</sup>, distance from midway between spines FF<sup>1</sup> to table top; KK<sup>1</sup>, measurement for distance of transverse diameter of inlet to table top; MM<sup>1</sup>, anteroposterior diameter of midpelvis.

the anteroposterior view, the feet should be together, with the toes pointing up. For the lateral view, it is best to center over the hips.

#### IV. TECHNIQUE OF MEASUREMENTS

The routine for obtaining the usual measurements is described below in the sequence which has been found most practical. Secure the "measured distance" and the "correction factor." If the slide-rule is to be used, set the arrow of the slide under the proper "correction factor," and set the movable hair-line over the proper "measured diameter." Read off the ana-

tomic or real diameter on the "corrected diameter" scale.

#### 1. True Conjugate

(Anteroposterior Diameter of Inlet)

On the lateral view: Measure the shortest distance between the anterior margin of the sacral promontory and the posterior margin of the symphysis. This is the "measured diameter" (Fig. 1, AA<sup>1</sup>).

To correct for distortion: On the anteroposterior view measure the distance between the greater trochanter limits, divide by 2 and subtract 3 (Fig. 2, BB<sup>1</sup>). We divide by 2 to obtain the distance from symphysis to greater trochanter. We subtract 3 cm. because experience has shown that it is enlarged to this extent on the film, as compared to measurement on the patient.

This number is now called the "correction factor."

#### 2. Anteroposterior Diameter of Mid-pelvis

On the lateral view: Draw a line along the posterior wall of the symphysis, continuing toward the obturator foramina. Draw a perpendicular to this line, from midway between the tip of the promontory and the sacrococcygeal joint. This is the "measured diameter" (see Fig. 1, MM¹).

To correct for distortion: Correction factor for this is the same as for the other anteroposterior diameters in the midline; that is, the same as for the true conjugate.

#### 3. Posterior Sagittal

On the lateral view: Draw a line backwards along the lower border of each obturator foramen (see Fig. 1, cc and c¹c¹). Where these lines pass through the posterior edges of the ischial rami, place marks. These points are taken as the ischial tuberosities. Mark the midpoint between them. Measure from this midpoint to the tip of the sacrum (see Fig. 1, DD¹). This is the "measured diameter."

To correct for distortion: Since this diameter lies in the same plane as the true conjugate, the same "correction factor" is used as was used for the true conjugate.

#### 4. Between the Ischial Spines

On the anteroposterior view: Measure the distance between the spines (Fig. 2, EE<sup>1</sup>). This is the "measured diameter."

To correct for distortion: On the lateral view, mark the two spines and the midpoint between them (Fig. 1, FF¹). Measure the shortest distance (Fig. 1, GG¹) from this point to the sacrum base line. The latter is a line drawn parallel to the film edge, touching the posterior border of the sacrum.

To correct the correction factor for distortion: (In the same way that we correct the original diameter, we can modify the correction factor when it is too much enlarged. This improves the final accuracy.) Since the above diameter (midpoint between spines to base line) is in the midplane of the pelvis, it may be corrected by the same factor as was used to correct the true conjugate. Using, therefore, the above diameter (midpoint between spines to baseline) as "measured distance," and using the correction factor for the true conjugate as "correction factor," derive the "corrected length." This measurement (the corrected length) is the "correction factor" for the bisischial diameter.

#### 5. Transverse of the Outlet

On the anteroposterior view: Starting at the brim of the pelvis, and running downward longitudinally through the outer border of each obturator foramen, there is a pronounced linear density, which appears as a heavy white line representing the lateral pelvic wall. With the crayon, extend these lines caudally, continuing their natural directions. Where the crayon lines pass through the caudal edges of the ischial rami, place marks (Fig. 2, HH¹). These points are taken as the ischial tuberosities. Measure the distance between them. This is the "measured diameter."

To correct for distortion: Since the transverse of the outlet and bisischial diameters ie close together, use the same "correction factor" as was finally used for the bisischial.

#### 6. Transverse of the Inlet

On the auteroposterior view: Measure the widest transverse diameter of the pelvic brim. This is the "measured diameter" (Fig. 2, JJ).

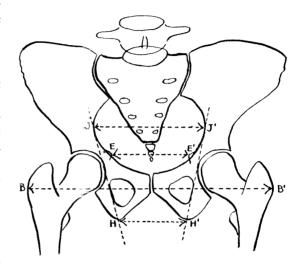


Fig. 2. Anteroposterior view of pelvis for locating measurements described in text. BB¹, diameter between greater tuberosities; EE¹, transverse diameter of mid-pelvis at spines; JH and J¹H¹, guide lines for locating the tuberischial points; HH¹, transverse diameter of pelvic outlet at tuberischial points; JJ¹, widest transverse diameter of pelvic inlet.

To correct for distortion: On the lateral view, draw a line from the promontory to the top of the symphysis. Mark the junction of the posterior and middle thirds of this line. Measure the shortest distance from this point to the base line used in correcting the bisischial diameter (Fig. 1, KK<sup>1</sup>). Subtract 2 cm. (because the true transverse plane lies below the anteroposterior plane of the inlet).

To correct correction factor for distortion: Since the above diameter (junction of posterior and middle thirds to base line) is in the midplane of the pelvis, it may be corrected by the same factor as was used for correcting the true conjugate. Using the above diameter (junction of posterior and middle thirds to base line minus 2) as "measured distance" and using the correction factor for the true conjugate as "cor-

rection factor," derive the "corrected length." This measurement (the corrected length) is the "correction factor" for the transverse of the inlet.

#### 7. Circumference of Fetal Skull

Step A. On the anteroposterior view: Measure the circumference of the skull skull circumference in the anteroposterior view.

Step B. On the lateral view: Measure the circumference of the skull, using the twirled adhesive. This is the "measured perimeter."

To correct for distortion: On the anteroposterior view, measure the shortest dis-

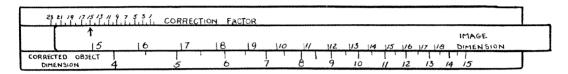


Fig. 3. Slide-rule, one face.

using the twirled adhesive. This is the "measured perimeter."

To correct for distortion: On the lateral view, measure the shortest distance from the approximate center of the skull to the same base line as was used for correcting the bisischial diameter.

To correct correction factor for distortion: Since the approximate center of the skull lies near the midplane of the pelvis, the

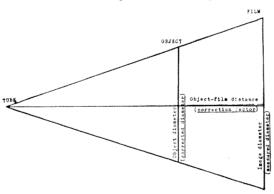


Fig. 4. Enlargement of the roentgen shadow.

same correction factor is used as was used for the true conjugate. Using the above diameter (center of skull to base line) as "measured distance" and using the correction factor for the true conjugate as "correction factor," derive the "corrected length." This measurement (the corrected length) is the "correction factor" for the

tance from the outer border of a trochanter to a line drawn through the approximate center of the skull and parallel with the long axis of the body. (Measure from the trochanter on which the patient was lying in the lateral view.) Subtract 3 cm. This is the "correction factor."

Step C. On the side of the slide-rule bearing red numerals, derive the "corrected perimeters" for Steps A and B, and average the two. This is a theoretical skull circumference, but conforms roughly to that measured post partum in the biparietal plane. Skin thickness is calculated into the slide-rule, so that the "corrected perimeter" scale reads skull circumference including skin.

(It is assumed that the fetal head did not move appreciably in relation to the pelvis between the taking of the anteroposterior and lateral roentgen exposures.)

#### 8. Age of Fetus

Place the movable hair-line over the determined skull circumference on the "corrected perimeter" scale. Read approximate fetal age on the lowermost scale.

#### V. COMMENTS

A routine has been presented for roentgen pelvimetry. It is designed for quick clinical use in obstetrics. It is based on simple geometry, and introduces a new instrument, with a much simplified technique. The instrument is a slide-rule constructed specially for this system of pelvimetry.

The method described has been evolved over the last several years in clinical use at two busy hospitals, where well over 500 cases were examined. In many instances, the true conjugate was checked against Thom's methods (a) in which the film is viewed as if by the target of the roentgen tube, and a plate of glass is placed in the plane of the patient's inlet, (b) in which a notched brass centimeter rule is fastened to the midline of the patient when the lateral roentgen exposure is made. The results were satisfactorily alike, while our measurements were more quickly and more easily obtained. The Ball pelvicephalometer was used in a series of cases, but difficulty was encountered in following the curved lines on the chart. A more serious objection to the Ball technique, however, is this: that volumetric measurements are computed. Not only have these proved unreliable as indices of disproportion, but linear measurements would seem to be preferable for the obstetrician. These he understands, and his clinical examination can be easily compared with the roentgen report. Although it is rather difficult to

measure a pelvis during cesarean section, we had this done on two occasions and were satisfied with the correlation. We have checked each of the measurements repeatedly on the dry skeleton, by taking roentgenograms with varying shifts of the tube. Theme is a liberal margin of safety in the placement of the pelvis, but it is important to obtain a fairly true lateral view. Despite our careful checking, we are aware that the highest degree of accuracy is not vet established, and for this reason we contemplate (and recommend to others who are interested) making roentgen examinations of cadavers for correlation with the true, anatomical measurements.

It is our hope that the simplicity and completeness of the method described will invite more clinicians and roentgenologists into the field of roentgen pelvimetry for guidance in their obstetrical problems. We feel that accurate and simple roentgen pelvimetry is a forward move towards reducing the number of cases which will be subjected to an unsuccessful or undesirable trial of labor. For it is our suspicion that mental disease statistics may someday show that every labor which concludes with a living baby is not necessarily, from all aspects, a "successful" one.

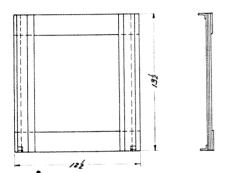


## THE BOOK-SHELF STEREOSCOPE

 $B_V$  J. J. SINGER, M.D.

From Rose Lampert Graff Foundation of the Cedars of Lebanon Hospital Chest Service LOS ANGELES, CALIFORNIA

IN ORDER to obtain the best view of a completed roentgenogram it is necessary to place the film before a properly illuminated box. It has been shown that various densities in the film can best be studied with a varying degree of light intensity. The illumination at the surface of the box should be approximately 2000 meter



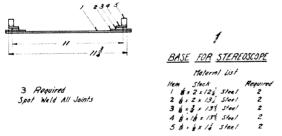


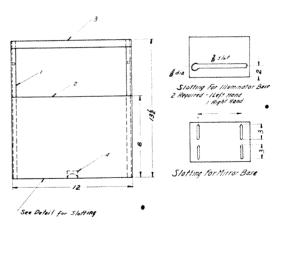
Fig. 1

candles (200 foot-candles). The light which emana es from the viewing box should be bluish-white in color. Single chest films are most frequently used in general work because of the lack of stereoscopic units and also for reasons of economy.

In many offices it is not always possible to find suitable space for a full-sized stereoscopic unit. In order to conserve space it occurred to me that I might build a stereoscopic unit into a bookcase so that the illuminator could be used either as single light source and by adding platforms with tracks the entire base of the bookcase could be made available for the apparatus. The drawings (Figs. 1, 2 and 3) show the plans and the type of material used.

The complete unit consisting of two illuminators and mirror can be arranged to fit into the 5-foot book-shelf of usual depth of 14 inches. The height of the second shelf should be 18 inches and should be set back  $6\frac{1}{2}$  inches to accommodate the illuminators when in the closed position.

The three units are mounted to the lower shelf, as shown in Figure 4, by mounting bases (Fig. 1) screwed to the shelf. The sliders (Fig. 2) fit into these bases and are provided with suitable stops to prevent being pulled out too far. The illuminators are mounted on the slider by a special base and support (Fig. 3 B and C). This base



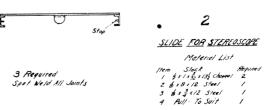


Fig. 2

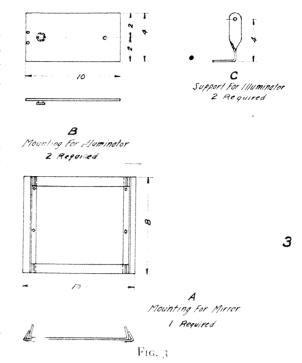
<sup>&</sup>lt;sup>1</sup> Weyl, C., and Warren, S. R., Jr. Apparatus and Technique for Roentgenography of the Chest. Charles C Thomas, Springfield, Ill., 1935, p. 54-

is made so that the illuminators can be entirely removed. The mirror mount requires an additional slide (Fig. 3 A) to bring the center line of the mirror in center line with the illuminator or film. This mirror mount can be made to suit other types of mirrors.

Operation. From closed position (Fig. 4) the slides are pulled out to maximum position. The illuminators are turned on their base to bring glass toward the mirror (Fig. 5). The mirror is placed on its slide and further pulled out and aligned with the illuminators.

The advantages of the book-shelf stereoscope are that it is simple in construction; it takes up very little space; and it is economical.

I wish to take this opportunity to thank Mr. K. F. Burkholder of the Westinghouse X-ray Company for many helpful suggestions in the development of the apparatus.



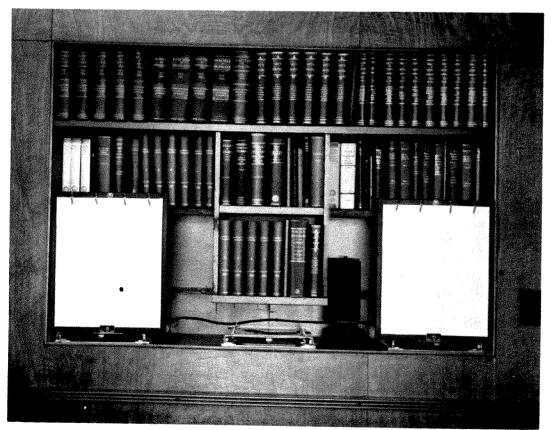


Fig. 4. Note the removable mirror behind the illuminating box on the right. The extension platforms are all telescoped in the base of the bookcase.

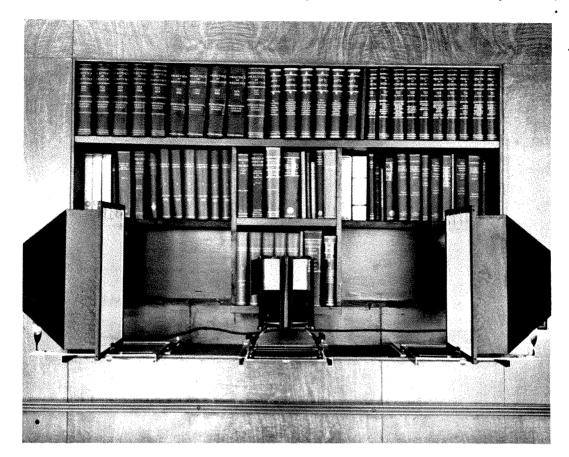


Fig. 5. Three platforms pulled out from the case. On the central platform note the mirror for stereoscopic use.



### THE FLUOROENTGENOGRAPH

By FRANZ J. LUST, M.D.
NEW YORK CITY

HE importance of fluoroscopy in the examination of the gastrointestinal tract is well recognized. The routine procedure of first fluoroscoping and then taking roentgenograms in different positions does not always satisfy. It often happens that certain types of movements of the stomach, duodenum or appendix are only seen during fluoroscopy. These conditions, partly physiological, partly pathological, cannot always be visualized by roentgenograms which are taken after fluoroscopy. Even if the fluoroscopy is interrupted to take a roentgenogram a certain time must elapse until all the switches are set and an exposure can be made. For many years certain devices have been on the market to improve our roentgenological work. I have only to mention those constructed by Baensch, Berg, Chaoul and others. Most of these appliances, however, work only in one position and most of them are constructed for exposures with the

For many years we have been working with these cassettes, the most popular of which is the one constructed by Berg. With this outfit four exposures are made on one film of the 18 by 24 cm. size. After two exposures are made, the cassette has to be taken out of the frame and put back after being turned upside down. As this has to be done while the fluoroscopic room is dark the procedure is a rather difficult one. Another feature is that the Berg frame cannot be used easily in the horizontal position. Some of the other attachments are expensive, clumsy or difficult to handle.

patient in the upright position.

In 1936 we therefore designed an attachment to overcome some of the difficulties of the former constructions. Our device, the fluororoentgenograph, is constructed as follows: there is a lead plate with an opening to the right of the middle. Toward the patient there is a round, semispherical part which serves for compression, toward

the examining physician a small fluoroscopic screen covers the opening of the lead plate. To the left of the fluoroscopic screen there is a cassette holder which during fluoroscopy is entirely protected by the lead plate. A cassette  $8 \times 10$  inches in size is placed in the holder. The cassette holder with the cassette can very easily be moved to the right between the opening

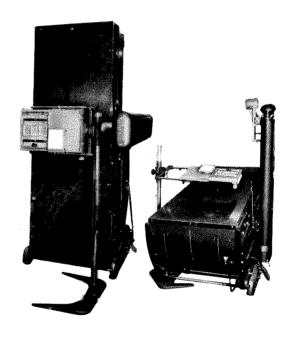


Fig. 1

in the lead plate and the fluoroscopic screen as the holder runs on a rail. We are therefore able to switch the cassette in its place in upright and in horizontal position. For the first exposure (right lower quadrant of the film), the holder with the cassette is arrested at the end of the fluoroscopic screen by a butten which being pushed releases the cassette so that the holder can be moved far to the right side and the second exposure (left lower quadrant of the film), can be made. A special device permits the

rotation of the cassette in the cassette holder so that the other side of the film can now be exposed in the same way. The entire fluororoentgenograph can be fixed on a stand (see Fig. 1) or exchanged with the normal fluoroscopic screen. There are special screws to move the fluororoentgenograph upwards and downwards, so that it can be fixed at any angle as needed for special work.

The advantages of our fluororoentgenograph are the following:

- (1) Cassettes of routine size (8×10 inches) are used.
- (2) There are four exposures on one film. Only one procedure is necessary for filling and developing.
- (3) The fluororoentgenograph can be used with any roentgemological outfit, in any position (horizontal and vertical).
- (4) The simplicity of construction enables easy, undisturbed work.
- (5) During the exposure we see on the fluoroscopic screen the part we are later to see on the film.
- (6) The rotating of the cassette is done

- *inside* the fluororoentgenograph. The cassette need not be removed.
- (7) The fluororoentgenograph can be manufactured easily by any skilled mechanic.

The fluororoentgenograph is especially useful for work in gastroenterology. Films taken during filling of the stomach, of the movement of the cardiac portion of the esophagus and stomach, the question of motility and peristalsis of stomach, pylorus and duodenum are fields in which this attachment will be most widely used. The duodenal cap in its different positions is especially easy to study. Films in the left oblique position to reveal changes in the anterior and posterior wall of the duodenum are easily taken. Until now it has often been difficult to visualize these parts as the stomach overlapped the cap in the left oblique position. The second part of the duodenum and the question of duodenitis can easily be studied. The same is true for the small intestine, appendix, colon and gallbladder. In our work on the mucosa of the colon we have already obtained good results with our technique.



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# RADIUM LITERATURE

#### ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

Kramer, Benjamin, and Halpert, Béla. Marble bones. 1. Clinicopathologic observations. Am. J. Dis. Child., April, 1939, 57, 795-808.

The authors report a case of the typical form of marble bones (osteosclerosis fragilitas generalisata, Laurell and Wallgren; Marmorknochenkrankheit, Albers-Schönberg; osteopetrosis, Karshner), with clinical, pathologic, roentgenologic and chemical data. Their case, as far as they could ascertain, was identical with a considerable number of those reported as to approximate age of the patient, the roentgenographic appearance of the skeleton and the clinical course of the disease, with blindness and fatal termination.

The post-mortem observations in their case suggest that the changes in the skeleton about the centers of ossification and the resulting pro-

duction of a faulty osseous structure were the principal lesions. The changes in the bone marrow were slight and secondary, so that the scattered blood-forming islands in the liver, spleen, kidneys and lymph nodes were perhaps remains from fetal life rather than part of a compensatory mechanism. Of the organs of internal secretion, the thymus, the thyroid, the parathyroid and the adrenal glands presented nothing unusual, nor could any morphologic changes be detected in the hypophysis cerebri.

Evidences of axitaminosis were present. The patient, three and one-half months of age, presented a degree of rickets which they had never seen in one so young. The rachitic changes were very resistant to therapy. They also felt there was some evidence of possible faulty utilization by the patient of the antiscorbutic factor. They do not infer that marble bones is itself a type of avitaminosis. The metabolic defect, whatever it is, confers on the patient susceptibility to certain avitaminosis, the manifestations of

which are modified by the lesion characteristic of marble bones, which not only produces morphologic changes but confers a state of refractoriness to appropriate therapy.

According to Schmidt it is desirable to separate the cases in which marble bones occur in infancy or in early childhood from those in which the condition appears later in life. He contends that in the adult type of the disease usually the changes in the blood-forming organs and the blood (osteosclerotic anemia) dominate the picture, while in the childhood type the skeletal changes are paramount. Indeed, in the latter type the changes in the osseous system are so progressive and severe that the afflicted children usually do not survive to reach complete skeletal development.—R. S. Bromer.

KRAMER, BENJAMIN, YUSKA, HENRY, and STEINER, MATTHEW M. Marble bones. II. Chemical analysis of bone. Am. J. Dis. Child., May, 1939, 57, 1044–1057.

The term "marble bones" refers to certain gross physical characteristics of the bone in osteopetrosis rather than to its actual chemical composition or to the crystal structure of its organic matter. Although several post-mortem examinations have been made in cases of this condition, few complete reports on the chemical composition of the bones are available. The authors' objective in their study was (1) to determine the chemical composition of the inorganic material (a factual aim); (2) to provide, if possible, an explanation for the peculiar properties of this bony mazerial, such as its roentgen and histologic appearance and its brittleness, and (3) to elucidate the mechanism of the disease.

They report the summary and conclusions of their study of a case of osteopetrosis as follows:

"The percentage of ash, of calcium and of phosphogus in the bones of an infant with osteopetrosis, where the characteristic lesion was present, was distinctly higher than in the corresponding bones of a normal newly born infant, except in the flat bones of the skull.

"The ratio of residual calcium to phosphorus was in harmony with the idea that the calcium-phosphorus compound in marble bones is tertiary calcium phosphate.

"In analyses of the upper and lower tibial epiphyses, evidence of a calcium-phosphorus compound having a lower ratio of calcium to phosphorus was obtained.

"When calculated in terms of acid-base equivalents, the total fixed base content as determined by electrodialysis exceeded the sum of the calcium and the magnesium content by 1.2 to 5.9 per cent. Part of this excess of base undoubtedly was represented by the sodium and potassium content of the bone. There is therefore no major basic component in marble bones which is not represented by the well known elements of calcium, magnesium, sodium and potassium.

"The value of n, i.e., the molecular ratio of calcium phosphate to calcium carbonate in the bones of the infant with osteopetrosis, was found to be approximately 2, corresponding to that found in normal adult bone or in the bones of rachitic infants, i.e., has more carbonate than bones of normal infants of the same age.

"There was a satisfactory agreement between the ash content as determined by heating dried fat-free bone at 500 C. and the ash content calculated on the assumption that calcium and magnesium exist as carbonates and that phosphorus is present as tertiary calcium phosphate. On the same assumption, determination of the acid-base balance showed a slightly positive base balance.

"The significant findings therefore are a higher carbonate content and hypermineralization. A high carbonate content is also present in adult and rachitic bone and may account for the increased fragility. Hypermineralization is a finding inconsistent with the diagnosis of rickets. It is therefore likely that the combination of high carbonate content and hypermineralization characterizes the mineral content of marble bones."—R. S. Bromer.

Atsatt, Rodney F. Acute osteomyelitis of a vertebral body following compression fracture. J. Bone & Joint Surg., April, 1939, 21, 346–352.

Atsatt reports a case of compression fracture of the body of the second lumbar vertebra. On this primary lesion was superimposed a secondary hematogenous infection which was localized within the fractured vertebral body. He believes that this is the first case to be reported of an acute osteomyelitis developing at the site of a recent compression fracture.

The hematogenous infection was caused by a streptococcus, possibly metastatic from a gingivitis. The treatment was conservative with sulfanilamide medication, which was apand Dadium Litanatura

parently successful until an overwhelming acute pyelonephritis deranged the patient's resistance and brought about a fatal termination.

Tuberculosis and the Charcot type of degenerative and reparative lesion of the spine had to be excluded in the differential diagnosis. Infective agents other than the streptococcus which were considered were the Bacillus typhosus, Bacillus melitensis, Staphylococcus albus and the pneumococcus. Post-mortem smears showed a few degenerate-appearing streptococci, and post-mortem cultures from the abscess (retroperitoneal, along the spine) proved the validity of the assumption that the Streptococcus beta haemolyticus was the invading organism, and indicated that the treatment had been correct as far as medication was concerned. The outcome with surgery might have been better, however.—R. S. Bromer.

Geschickter, Charles F., and Maseritz, I. H. Skeletal metastasis in cancer. J. Bone & Joint Surg., April, 1939, 21, 314-322.

This article is based on a collection of 5,739 cases of carcinomata arising from various organs. Its purpose, the authors state, is to emphasize the incidence of skeletal metastasis in which there is no clinical evidence of a primary lesion, and to submit other data relative to osseous invasion by metastatic carcinoma. There were 356 cases in which carcinomata metastasized to bone. The primary source of the metastasis was definitely determined clinically in 296 instances. In 60 cases, or 16.8 per cent, however, there was no clinical evidence as to the source of the primary growth. The first indications of disease in this group of metastases of unknown origin were symptoms referable to the skeletal system. "Rheumatic pain" was a common complaint, and in several instances the patients were treated for arthritis. In I case a mass was palpated in the neck, and this later proved to be a lymph-node metastasis; in the remaining 59 cases there were no subjective or objective findings referable to other systems. Pathological fractures occurred in 19 instances, or 31.6 • per cent, and solitary lesions in 34, or 56.6 per cent. The bones involved, in order of frequency, were: femur, spine, humerus, pelvis, ribs, skull and other bones to a lesser degree. The diagnosis in each instance was dependent on microscopic study of sections removed at

biopsy. In sections with typical histological changes of hypernephroma, it was possible to determine the source of the metastatic lesion on the microscopic evidence. In the remaining cases a diagnosis of metastatic carcinoma could definitely be made from the sections, but no opinions were ventured as to the possible sources of the lesions.

The roentgenographic changes in metastatic carcinoma vary. The lesion is often solitary and may simulate many types of bone affections. It may present a localized area of osteoporosis and resemble the osteolytic variety of osteogenic sarcoma, or a patchy sclerosis and resemble the sclerotic type. Similarly, multiple lesions of carcinoma may simulate those of Hodgein's disease, the leukemias, and multiple myel ma, making it impossible to differentiate the various affections roentgenologically. Ewing's sarcoma, chronic osteomyelitis, syphilis, tubesculosis, osteitis fibrosa cystica, and other tumers of bone may closely resemble lesions of carc moma.

The prostate is the most common source of skeletal metaetasis; the breast, second; the kidney, third, while the stomach, lung, thyroid and other organs are involved less frequently and in the order given. The size of the primary lesion is no index of the probability of metastasis. Metastatic involvement of bone may occur many years following the primary operation, and in the series reported in this article, breast cancer ekeletal metastasis was observed as late as 18.25 years postoperatively. Irradiation of the osseous lesions relieves pain and prolongs the like of the patient.—R. S. Bromer.

RANKIN, JOHN O. Adamantinoma of the tibia. J. Bone & Joint Surg., April, 1939, 21, 425-432.

Adamantinoma is an epithelial tumor which arises from the enamel organ of the teeth and ordinarily occurs in either the maxilla or the mandible. These have been reported a comparatively large number of cases in this location. Occasional cases of the condition occurring in the region of the pituitary gland have been recorded. One case involving the ovary has been reported by Thoma. In the remaining reported cases the adamantinomata have occurred in the tibia. The author's case is the eleventh instance of its occurrence in the tibia reported in the general literature and the sixth to be found in the American literature.

The theories of the etiology of tibial adamantinomata are very intersting, but by no means proved at the present time. In general, two theories have been advanced. The first is that from early fetal life there has been a cell-rest in the tibia, which becomes activated in later life to form one of these tumors. The second is that, due to trauma or for some other reason, epithelium is implanted into the periosteum and later develops into adamantiromatous tissue.

Clinical and roentgenographic examinations are insufficient for establishing a diagnosis. Even on histological examination the diagnosis is not clear-cut, as is shown in the author's case and in other reported cases. Adamantinoma is a slow-growing tumor, which coes not metastasize, but recurs unless completely removed. The time of recurrence varies from a few months to several years. Rankin believes that, if the growth is not too extensive, it can be removed completely at the first operation by radical saucerization and curettement. If a second operation is necessary, the operation which he describes in this paper is certainly superior to an amputation.

The roentgenographic appearance of the lesion in the tibia was an intramedullary, multilocular expanding tumor without any proliferation or thickening of the periosteum.—

R. S. Bromer.

KLEINBERG, SAMUEL. Malignant giant-cell tumor of bone. J. Bone & Frint Surg., April, 1939, 21, 433-441.

Kleinberg states that it has been variously estimated that from 3.5 to 15 per cent of giant cell tumors of bone undergo malignant change. Sufficient evidence, he believes, has now accumulated in the literature to emphasize this unfortunate possibility. If a g ant cell tumor is not treated and continues its natural development, as many did several generations ago before the opportunities for treatment were appreciated, it may spontaneously regress and disappear, but in the majority of cases it increases in size and the patient succumbs from hemorrhage or sepsis. In no instance of an untreated case is there a record of the appearance of malignancy or pulmonary metastasis. However, in recent years, few, if any, such tumors go untreated, and many are subjected to vigorous, repeated, and not infrequent y often repeated treatments. The supervention of malignancy has been recorded only in such treated cases.

It is admitted that the customary conservative methods of irradiation or surgery, alone or combined, are successful in the majority of cases, but Kleinberg thinks malignant transformation in the remainder should be prevented if possible.

A reasonably accurate diagnosis, without biopsy, can be made, based on the history, age of the patient, location of the lesion, and the roentgenographic appearance. These elements suffice in the majority of cases, but, because of the fact that they are variable, a positive diagnosis is not really possible without a biopsy. In the author's experience, he cannot recall a single instance of either a benign or a malignant tumor in which a simple, surgically well planned biopsy has caused any untoward symptoms, aggravation, or progression of the disease.

In his patient the lesion was located in the distal end of the tibia. From the history of the comparatively long course of the illness Kleinberg assumes that it was originally a benign giant cell tumor. It is difficult to speculate, he says, when malignancy set in. Although there was a history of injury subsequent to which the patient became acutely aware of the tibial lesion, yet for months previously he had frequently felt a twinge of pain in the leg. As the patient indulged in many athletic sports, perhaps he had injured the leg on many occasions and in that manner had stimulated the malignant change. It may be permissible to believe that the lesion may have had a low grade of malignancy originally, which was further attenuated but not entirely destroyed by intensive irradiation, and that subsequent minor traumata excited a full development of malignancy. Appreciating that many giant cell tumors of bone have been cured by irradiation, nevertheless Kleinberg feels that a more satisfactory procedure in his case, which was readily accessible to surgery, would have been thorough removal of the tumor tissue, supplemented by cauterization of the wound. This was advised by the surgeon, originally consulted by his patient. Knowing through abundant evidence, that a giant cell tumor of bone may become malignant and prove fatal, he is convinced that when a giant cell tumor can be treated surgically it should be completely excised at the earliest opportunity. Furthermore, in order that there shall be no doubt about the diagnosis, which cannot be diagnosed with certainty from the roentgenographic appearance alone,

biopsy ought to be performed in every accesible lesion which may be a giant cell tumor. The believes irradiation should be reserved for iant cell tumors of inaccessible bones.—R. S. Bromer.

#### BLOOD AND LYMPH SYSTEM

DIMTZA, A., and JAEGER, W. Arterielle Obliterationen der unteren Extremitäten bei der Arteriosklerose und bei der Endangitis obliterans. (Arterial obliterations of the lower extremities in arteriosclerosis and endangitis obliterans.) Fortschr. a. d. Geb. d. Röntgenstrahlen, July, 1939, 60, 65-68.

These observations are based on 200 cases taving "total arteriograms." The technique onsists in the use of a film 20×90 cm. in size. vhich is exposed in two sections. The upper alf nearer the site of injection is exposed first vith the lower half covered, then when the ontrast medium has reached the lower leg he procedure is reversed. Thorotrast is preerred to the organic iodine preparations and 10 injurious effects of its use have been oberved. Arteriosclerotic vessels usually appear lilated and tortuous with irregularities of the nner wall which may contain calcium. The ressels of endangitis appear straight and narow with smooth walls and spindle shaped constrictions. In Raynaud's gangrene there is 10 alteration of the large vessels. True obstrucion due to disease of the vessel wall is recogtized (1) when there is a sudden interruption of the vessel lumen, (2) when the interruption nas a sharp border and shows no dilution of the nedium and (3) when the interruption coresponds to evidence of a collateral circulation. The extent and size of the collateral circulation s an index of the duration of the obstruction. The number, form and extent of the obstrucions are not characteristic but obstructions lue to arteriosclerosis tend to occur in the ower femoral and popliteal arteries while those of endangitis obliterans are more common in the upper portion of the femoral artery. Surgical extirpation of the obstruction together with other conservative measures yields good results.-W. A. Evans, Jr.

#### ROENTGEN AND RADIUM THERAPY

NITZGE, K., and IVEN, H. Über die Protrahierung der Röntgendosis. (Protraction of the roentgen dose.) *Strahlentherapie*, 1938, 62, 91–108.

The question of dosage of roentgen rays has been studied for a long time on plants of various types. These authors also utilized plants for their studies which were carried out between 1934 and 1938. The plants were tobacco, tomatoes, sova beans, maize, dry seeds and germinated tissae. When the protracted dose was used it was found that for dry seeds there was obtained a simple summation of the dose according to the Bunsen-Roscoe law while for germinated tissue the Schwarzschild's law was found applicable. Most of the experiments were carried out on tobacco which was found especially suitable for this purpose, in consideration of the long observation periods of two to three months necessary when this method is employed.

In the irrad ation of germinated tissue numerous constantly recurring, and therefore typical accompanying phenomena associated with a disturbance in growth were observed. In the maize experiments peculiar changes of the condition of the blossom and fruits as well as a splitting of the fruit bulbs were found. Some growth deviations were observed which could be produced also by other external factors such as manuring and heat or by internal factors such as bastardization.

In the tobas co largely employed for these experiments a series of anomalies were demonstrable depending on the degree of roentgen dosage. The germinal layers presented only slight changes. On the buds, however, even minute doses produced anomalies which, when followed up by irradiation with larger doses, developed into pronounced striking deformities. On the basis of the results obtained from a study of the protracted effect of roentgen rays on tobacco and other plants it may be stated that the results clearly show the significance of a further follow up study of the injuries resulting from the irradiation as contrasted with the injuries resulting from a single irradiation. This type of study is especially valuable for the determination of the protracted fractionated roentgen dose. It will be desirable to carry out similar experiments on other types of plants, but even these limited experiments are of great significance for dally practice where roentgen irradiation is used.—A. S. Schwartzman.

Jovin, I. Die Behandlung des metastatischen Krebses der Halslymphdrüsen. (Treatment of metastatic carcinoma of the cervical lymph glands.) Strahlentherapie, 1938, 62, 262–286.

and then operation. External radium or roentgen therapy for technically operable cases but where the operation cannot be carried out because of poor general condition. Postoperative irradiation in each case.

Group III. Radium or roentgen therapy.—
A. S. Schwartzman.

GAJZAGO, E. Die Bedeutung der Röntgenschwachbestrahlung in der Gynäkologie. (The significance of weak roentgen radiation in gynecology.) *Strahlentherapie*, 1938, 62, 167–173.

In gynecology there are three indications for the inflammation inhibiting roentgen irradiation: mastitis, thrombosis and adnexitis. Of these three diseases best results are obtained from the roentgen radiation in the treatment of mastitis. The significance of these favorable results is accentuated by the fact that mastitis is a very frequent affection. It is generally known that the sensitiveness of the functional mammary gland towards pyogenic organisms is increased especially since a milk congestion alone is sufficient for the production of an affection. The danger is increased as a result of the fact that during breast feeding the nipples may not be properly cared for; cracks develop which serve as a portal of entry for the pyogenic organisms; because of the above, mastitis is a very frequent disease.

Roentgen irradiation of mastitis was employed for the first time about fifteen years ago Heidenhain and Fried were the first to mention the roentgen treatment of inflammatory diseases at the German Surgical Congress in 1924. Since then the subject has been extensively studied by many authors. In the course of the last seven years this author carried out 150 irradiations of the mammary gland. The dose used per radiation field of 8×10 cm. up to 15×15 cm. square, was 50 to 150 r, individualized according to the depth of the disease focus. This dosage would come under the designation of "weak" radiation.

Even though the nature of the effect of these rays is not clearly known, nevertheless in most of the cases treated a curative effect was obtained. As yet no satisfactory explanation can be offered in regard to the mechanism of action. Under the influence of the roentgen irradiation there occurs an immediate or very prompt disappearance of pain. Together with the above there occurs an improvement of the general

- 1. Not all palpable glands are carcinomatous; on the other hand, a metastasis may remain non-palpable for a long time. The clinical examination therefore permits a recognition of the true character of the glands only in a small percentage of the cases; in consideration of the above, one must assume the existence of a metastasis and the cervical region should be treated even where there are no palpable glands.
- 2. The necessary prophylactic treatment of Group 1 must be recognized. The methods employed vary. Surgeons recommend an extensive operation; radiologists, on the other hand, do not favor this disfiguring operation and such pathologists as Ewing support this view. Jovin varies his procedure from case to case depending on the type of primary tumor, on the general condition of the patient, on the cure of the primary tumor, etc. This method of procedure, however, requires great clinical experience.
- 3. The method of treatment of cases belonging to Group II varies in the different institutions. Quick, Bervin and other American authors recommend postoperative irradiation; Simons and Fischel do not advise postoperative irradiation. At present most authors use the surgical method of treatment of glandular metastasis preceded by radiation treatment. The operation must be carried out under the rules of cellular asepsis; it must be sufficiently extensive in order to permit the removal of the muscles, aponeurosis, vessels and glands "en bloc." Jovin is of the opinion that the postoperative irradiation is very useful and should be systematically employed.
- 4. Most authors agree as to the method of treatment of carcinoma of Group III. In these cases the operation is useless and actually dangerous. The chance of a successful post-operative irradiation following an incomplete operation is minimal. Only exceptionally is it possible to decrease inoperable glands by irradiation and render them operable. In cases of this type radiation therapy alone must be resorted to as a palliative measure. The following principles are recommended by this author for the treatment of glandular metastasis in the region of the neck:

Group 1. Observation, external radium or roentgen therapy, operation, operation and irradiation, depending on the given case.

Group II. Operation. In border line cases of operability, irradiation before the operation

its volume and a spherical contour in the presence of satisfactory collapse of the surrounding lung, and particularly if it should seem to increase in diameter, obstruction of its bronchus may be suspected. This has been called the "tension" or "tennis ball" cavity.

wheezes and rales, the last being coarse in the axilla and base; sputum 40-50 gm. daily (excessive for extent of apparent lesion), positive; vital capacity 1,800 cc.

Bronchoscopy (Dr. Samson), August 30, 1935: Active ulcerative tuberculous tracheobronchitis with slight stenosis of the left bronchus at its orifice.

TABLE I

	CLINICAL SYMPTOMS									
ROENTGENOGRAPHIC CHANGES	Rhonchi	Cough only	Cough and Dyspnea	Cough and Wheeze	Cough, Wheeze and Dyspnea	Cough, Wheeze and Cyanosis	Cough, Wheeze, Dyspnea and Cyanosis	Total Fre- quency		
Atelectasis	6	13	I	6	5	1	3	30		
Spontaneous intermittent										
atelectasis	2	1	I	I	2	0	0	5		
Extent of roentgen pathology not compatible with clinical course Degree of collapse greater	6	4	0	2	2	0	2	10		
than expected from evi-			_		Para					
dent lesion	3 1	- 3	2	5	*	0	1	13		
Sudden increased atelecta-				_			_	•		
sis with collapse therapy Visible changes in bronchi	5(11)	o 6(2b)	0	2	1 2 ( 1.1	0 (11)	ı	4		
Oechsli sign	5(1b) 2	2	0	3	5(1p)		0	13		
"Tennis ball" cavity	2	I	0	2 I	i	0	0	5 2		

<sup>(1</sup>b) indicates number of patients having had bronchograms.

In illustration we present the following cases from this series:

• I. Minor roentgenologic evidence of pulmonary tuberculosis with persistent positive sputum rhonchi, wheeze and dyspnea.

Case I. G. B., female, aged thirty-seven, No. 366737 (Barnwell, Littig and Culp's Case 6). "Influenza," January, 1935, with cough and fever to 102° F. Cough persisted, slightly productive. Tubercle bacilli were reported by her referring physician in May, 1935, although chest roentgenogram was said to have shown no lesion. Huskiness of voice, shortness of breath and "rattles" in the chest had been noted for a month before admission (August, 1935).

Roentgenogram, August 14, 1935 (Fig. 1a): Minimal pulmonary tuberculosis, left apex.

Physical examination on admission revealed palpable rhonchi over the left chest, with

Roentgenograms: September 17, 1935 (Fig. 1b): parenchymal infiltration (possibly an early lesion) appeared in the left mid-axilla, 3rd-5th ribs, as well as the former lesion in the 1st interspace, anteriorly. October 18, 1935 (Fig. 1c): mediastinal shift to the left, parenchymal lesion not changed. This suggested an early obstruction of the bronchus. November 11, 1935 (Fig. 1d): gross atelectasis of left lung. The patient had described a left pleuritic pain, three days previously. Sputum 30 gm. daily, positive.

Comment. This case demonstrates the rapid changes which may occur, although upon the initial examination a relatively minor lesion was in evidence. Roentgen therapy had been administered in September and again on November 7. It probably had little to do with the changes observed.

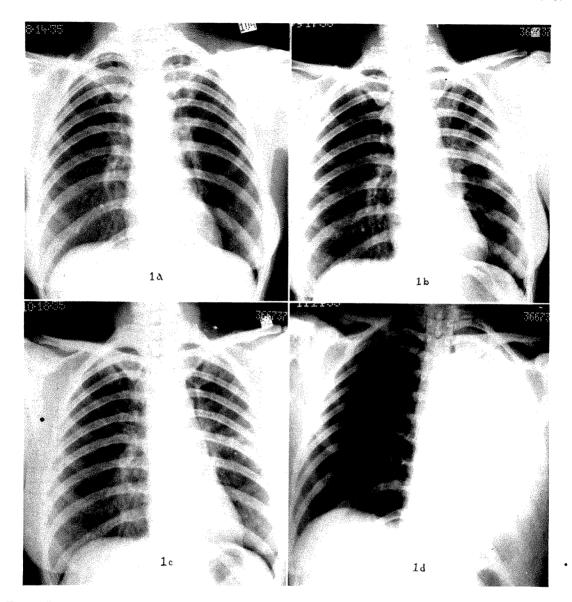


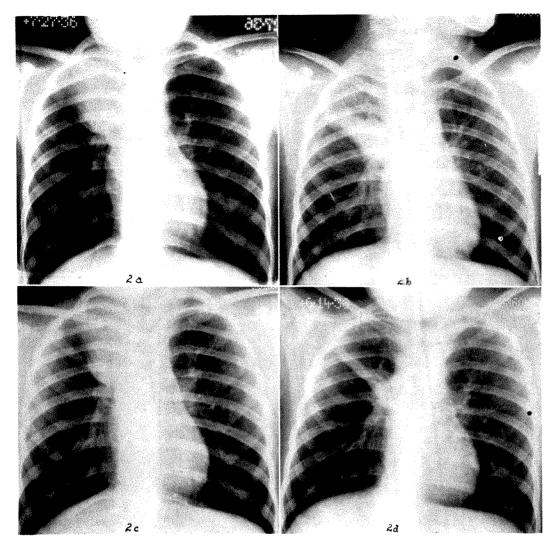
Fig. 1. Case 1. a, August 14, 1935: minimal pulmonary tuberculosis, left apex. b, September 17, 1935: parenchymal infiltration, possible early atelectasis, left 3rd-5th ribs in the axilla, in addition to former lesion in the apex. c, October 18, 1935: mediastinal shift to the left, parenchymal lesion not markedly changed; suggestive of early bronchial costruction. d, November 11, 1935: gross atelectasis of left lung.

(This patient is now dead; pneumothorax was induced with good response for a few months. Then followed periods of bronchial obstruction with high fever, relieved by evacuation of the retained secretions through the bronchoscope Terminally the disease ruptured into the pleural space, resulting in an empyema, bronchopleural fistula and death.)

#### II. Spontaneous intermittent atelectasis.

CASE II. D. K., male, aged nine, No. 386044. A school survey reported a positive tuberculin skin test in the spring of 1935, and "chronic fibroid tuberculosis" in a chest roentgenogram of August 1, 1935. (This film was not available for comparison.) Admitted July 26, 1936, for treatment of tuberculosis of the left hip joint.

No signs or symptoms of pulmonary tuberculosis were noted in the history (save the



• Fig. 2. Case 11. a, July 27, 1936: atelectasis of superior lobe. b, January 18, 1927: partial re-aeration. c, March 30, 1937: recurrent atelectasis. d, June 14, 1938: re-aeration.

roentgenologic report and diagnosis). No record s to be found of stomach washings or sputum naving been obtained or examined. (However the roentgenologic changes are almost classical for this type, hence the inclusion here.) Roentgenograms of July 27, 1936; January

Roentgenograms of July 27, 1936; January 18, 1937; March 30, 1937; and June 14, 1938 (Figs. 2a, b, c, and d, respectively) demonstrate the fluctuating at electasis of the right superior obe. There was unquestioned evidence of loss of aeration, reduced volume with shift of the accessory fissure upward followed by partial re-aeration and improved volume. The atelectasis recurred followed by subsequent re-aeration. It is improbable that an hilar adenopathy could have induced such changes, par-

ticularly without evidence of such nodular mass upon the roentgenogram.

This case must therefore be considered as one of stenosis of the superior bronchus, probably of the hyperplastic type of tuberculous bronchitis.

III. Excessive reduction of volume and air content with collapse therapy, in reference to the extent of roentgenographic evidence of disease.

(a) Following phrenicectomy:

Case III. L. H., female, aged twenty-seven, No. 309768 (Barnwell, Littig and Culp's Case 4). Ease of fatigue and weakness for two to three years had been accompanied by attacks of wheezing, dyspnea and cough for the last

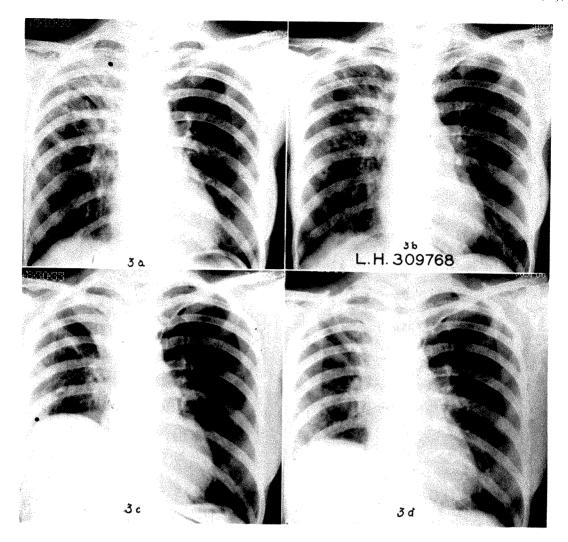


Fig. 3. Case III. a, March 10, 1933: moderately advanced right pulmonary tuberculosis; partial atelectasis of the superior lobe, right. b, March 29, 1933: some improvement in aeration. c, August 30, 1933: intereased atelectasis ollowing phrenicectomy. d, September 29, 1933: some improved aeration of superior lobe, but persistent atelectasis of median apical segment.

eighteen months. All symptoms increased during the two months prior to admission.

Upon examination there were rhonchi, râles and friction rub in the right thorax with dullness in the posterior apex; 5–10 gm. sputum daily, positive for acid-fast organisms, although they were not numerous.

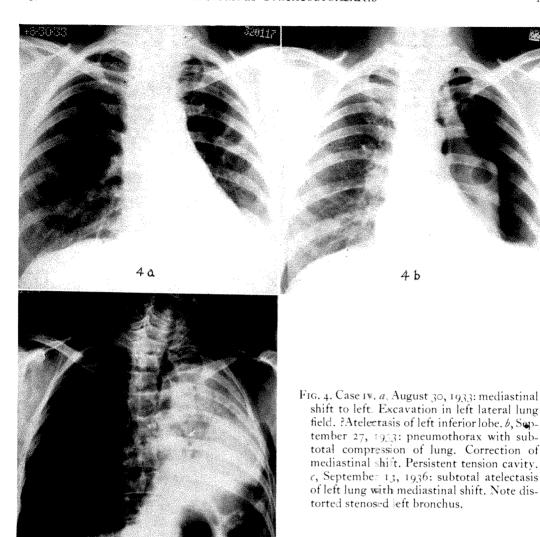
Roentgenograms: March 10, 1933 (Fig. 3a): moderately advanced right pulmonary tuberculosis with elevation of the accessory fissure, partial etelectasis of the superior lobe. March 29, 1932 (Fig. 3b): some improvement in aeration.

Right temperary phrenicectomy, April 11,

1933, was followed by a sharp recurrence and increase in the atelectasis of the superior lobe. The symptoms did not improve, although the sputum for a time contained no acid-fast bacilli. (A rapid shift from positive to negative sputum in the presence of moderately extensive tuberculosis must suggest a block of the bronchus from the involved area.)

Roentgenogram of August 30, 1933 (Fig. 3c) • demonstrates the atelectasis of the period following the phrenicectomy.

Bronchoscopy, September 6, 1933: extensive tuberculous tracheobronchitis with stenosis of the right bronchus, some stenosis of the left but



dmitting the bronchoscope. Several small ulerative lesions along the thickened mucosa.

Roentgenogram of September 29, 1933 (Fig. d) revealed some improvement of the aeration 1 the superior lobe, but a persistent atelectasis f the median apical segment.

Symptoms were somewhat improved after ne expectoration of a bronchial plug, about 7 nm. in diameter, early in October.

Comment. The clinical and roentgenoogic signs correspond rather closely in this ase. The patient obtained greater benefit s regards alleviation of symptoms after ronchoscopy than from the phrenicecomy. In this case, also, there was bronchoscopic evidence of left bronchus involvement with no gwoss roentgenographic evidence of material change, a not uncommon feature of the disease. (The patient was last seen in the summer of 1938. She had no cyanosis, looked well. Right upper lobe was still reduced in volume, but improved in aeration. Right diaphragm high but functioning with imited excursion.)

(b) Continued subtotal atelectasis of a whole lung following abanconment of a pneumothorax, tension or "tennis bad" cavity:

Case IV. M. L., female, aged fifty-four, No.

320117. No record of physical findings at time of initial roentgenogram.

August 30, 1933 (Fig. 4a): heart and mediastinum shifted to left with some elevation of the left diaphragm, thin-walled, spherical cavity in the lateral lung field, plane of the second interspace and third rib, anteriorly. Atelectasis of left inferior lobe suggested on the films, not positively demonstrated at the time.

September 27, 1933 (Fig. 4b): pneumothorax had induced a subtotal atelectasis of the lung, some apical adhesions suspended it from the pleural dome. The mediastinal shift was corrected. Although there were no evident adhesions arising over the cavity to suspend it, and it had shifted in position with the lung in collapse, the cavity maintained its size and spherical or "tennis ball" contour. (This type of excavation, with insufficient peripheral infiltration to produce a rigid wall, we now believe to be suggestive of bronchial obstruction.)

Pneumothorax was lost when the patient returned home, refusing further hospitalization or sanitarium care, the upper lobe re-expanded but not the cavity.

In July, 1935, a left temporary phrenicectomy was accomplished, the sputum becoming negative for a time, but the patient subsequently complained of cough and wheezing. A rapid reduction in volume of the superior lobe as well as the lower was observed at that time, arousing suspicion of bronchial obstruction.

She returned in March, 1936, with complaints of cough and wheezing following a "cold" accompanied by sore throat, pleuritic pain and blood-streaked sputum the preceding month. The entire left chest was dull, with decreased breath and voice sounds and tactile fremitus. A few post-tussive râles were heard. The sputum was again positive.

Bronchoscopy, March 14, 1936, revealed an ulcerative and partially stenotic left tuberculous bronchitis.

She made an uneventful recovery from a cholecystectomy for cholecystitis with chole-lithiasis in July, 1936. Sputum was positive at that time, but she refused any chest therapy. Vital capacity 1,300 cc., sedimentation index 0.9 mm. per minute.

The roentgenogram of September 13, 1936 (Fig. 4c) presents a gross shift of the mediastinum into the left hemithorax, elevation of the left diaphragm and subtotal atelectasis of the left lung. The distorted, stenosed left

bronchus is visible by virtue of its air content in the compact airless lung.

Comment. In retrospect, the tuberculous bronchitis should have been suspected in 1933 because of the atelectasis. The later disappearance of the cavity was probably the result of the completion of its bronchial stenosis during the period of the pneumothorax.

(c) Compression of lung about multiple thinwalled cavities by pneumothorax, persistence of sputum, subsequent demonstration of bronchial stenosis.

Case v. W. B., male, aged twenty-one, No. 345722. Ease of fatigue, chronic "cold" for one year, accompanied by a dry cough becoming productive three months before admission. Loss of 20 pounds in weight. Physical examination reported negative, except for grossly tenacious, purulent sputum containing 25–100 acid-fast bacilli per high-power field.

Admission roentgenogram, September 24, 1934 (Fig. 5a): multiple, thin-walled cavities withother minimal parenchymal and peritruncal infiltration in the left lung. Far-advanced pulmonary tuberculosis, left.

Pneumothorax, instituted early in October, compressed the lung about these cavities, which retained their size and spherical contour for some time (Fig. 5b, October 10, 1934).

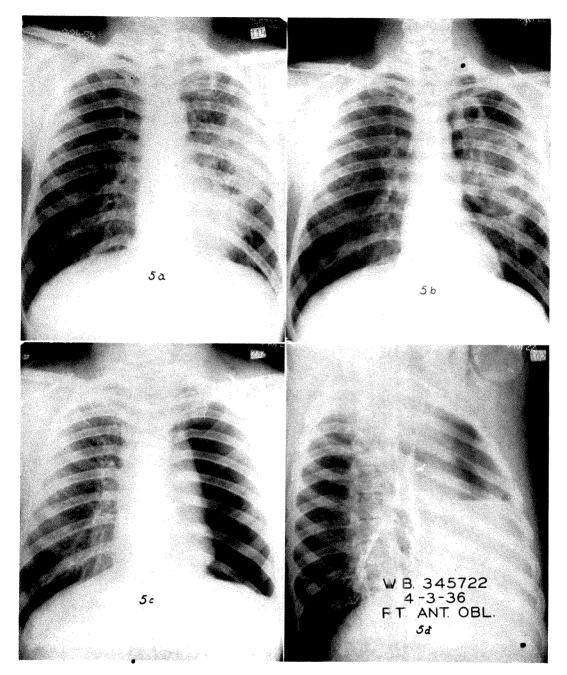
Although the patient gained weight, and the lung was progressively compressed under sanitarium care, the sputum remained positive and of the same quantity, Subtotal atelectasis of the lung was demonstrated in the roentgenogram of April 17, 1935 (Fig. 5c).

Bronchoscopy on August 3, 1935, revealed marked, pliable, exuberant granulation tissue, bleeding readily, in the left bronchus, whose lumen was reduced to 5 mm. or less.

Concentrated sputum specimens remained positive, and in April, 1936, the amount of sputum had increased with increase in numbers of bacilli. Cough had increased.

Bronchogram on April 3, 1936 (Fig. 5d) demonstrated the marked stenosis of the left bronchus just distal to the carina tracheae, with more or less deformity of the lumen of the lesser bronchi. The lung remained compressed. Considerable effusion had developed in the pleural space.

Throughout the subsequent course of the patient's illness, his recurrent periods of in-



16. 5. Case v. a, September 24, 1934: far advanced left pulmonary tuberculosis with multiple apparent cavities. b, October 10, 1934: persistent multiple excavations with remaining lung compressed about them by pneumothorax. c, April 17, 1935: subtotal atelectasis; sputur still positive. d, April 3, 1936: bronchographic demonstration of stenosis of left bronzhus.

reased malaise and elevation in temperature zere relieved by bronchoscopic drainage of the tenotic left bronchus. Ulceration was observed n December 2, 1936.

Comment. The apparent minimal in-

volvement of the lung in the early period (except for the encavations), the persistence of the spheroid contour of the latter after pneumothorax was instituted with greater initial compression of the relatively unin-

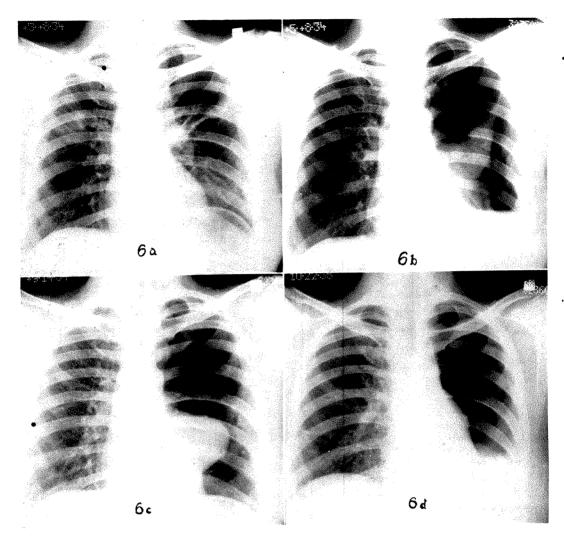


Fig. 6. Case vi. a, March 8, 1934: minimal parenchymal lesion, left mid-axillary lung. b, May 8, 1934: marked compression of left ling by pneumothorax; interpleural adhesions. c, August 8, 1934: re-expansion of inferior lobe following pneumonolysis, but increased dyspnea. d, October, 1935: subtotal atelectasis; wheezing persisted.

volved parenchyma than then excavated, the persistence of sputum in amount and character in spite of this collapse are strongly suggestive of pronchial involvement.

(d) Minimal evident parenchymal lesion, relatively excessive de-aeration of lung and increase of symptoms with collapse therapy.

Case vi. L. G., female, aged thirty-three, No. 323608 (Barnwell, Littig and Culp's Case 5). Fatigue and cough for seven months following a "cold," with fever and right sweats. Increase in cough, with sputum, right pleural pain and loss of weight for the pas: four months.

On admission the patient had a tuberculous

laryngitis. The sputum was positive. Expansion of the two sides of the thorax was equal, percussion note slightly impaired over the left apex, occasional râles were heard in the axilla, and the patient was aware of wheezing respiration.

Roentgenogram of March 8, 1934 (Fig. 6a) demonstrated a minimal parenchymal lesion in the left upper mid-axillary lung field.

Upon induction of pneumothorax (with some difficulty due to an angioma of the axilla—note calcareous deposits in the left thoracic wall), a marked compression of the entire left lung ensued (Fig. 6b, May 8, 1934). This was out of proportion to the previous apparent extent of the parenchymal involvement.

Following intrapleural pneumonolysis (Au-

gust 8, 1934) the inferior lobe re-expanded, but the patient's dyspnea increased.

The larynx had begun to improve in June. Wheezing respiration continued.

Bronchoscopy on January 12, 1935, revealed ulceration of the left bronchial mucosa with granulation tissue, exudate and multiple tuberculomata. Further bronchoscopy on February 7 suggested that the ulcerative lesions began about 2.5 cm. below the carina in the left bronchus.

Sputum varied from 12 to 40 gm. daily, positive on direct smear until August, 1935. A series of daily sputum examinations in November, 1935, was negative for tubercle bacilli on several days. Roentgen therapy had no appreciable effect.

In October, 1935, there was again a subtotal atelectasis of the left lung with some pleural effusion (Fig. 6d). (The patient is still alive with hydropneumothorax. Wheezing has persisted.)

Comment. The roentgenographic evidences of disease on the initial study were disproportionate to the sputum and symptoms. The massive compression of the early pneumothorax, the increase of dyspnea in the presence of re-expansion of the inferior lobe following the pneumonolysis, and the later re-collapse of the inferior lobe, with fluctuation of the sputum between positive and negative, subsequent to the section of the adhesions, and full collapse of the superior lobe in August present an epitome of the findings common to this complication of pulmonary tuberculosis.

#### DISCUSSION

The character of the excavations within the tuberculous lung is of importance. The presence of the tension or "tennis ball" type of cavity, to which we have alluded above, is suggestive of intracavitary tension by valvular obstruction of its bronchus, hence theoretically it should be more common in patients with tuberculous bronchitis.

The often relatively minor roentgen evidence of parenchymal disease in the presence of advanced tracheal and bronchial tuberculosis must also be emphasized. Here the sputum and the complaints of cough,

wheeze and dyspnea, with more or less cyanosis are important, and may refute the opinion of a minimal lesion gained from roentgenograms. Also, as we have noted in the cited cases, sudden disappearance of sputum or marked fluctuation in amount of sputum should suggest bronchial block.

We have seen in this group varying degrees of airlessness of lung, from rapid progressive loss of pulmonary air content and volume, through fluctuating periodic airlessness to persistent subtotal collapse or complete atelectasis. These several stages have been accompanied by more or less mediastinal shift (dependent upon degree of de-aeration and previous fixation of the mediastinum) and elevation of the diaphragm on the side of greater involvement.

In uncomplicated collapse by means of intrapleural pneumothorax, the lung should retain its ordinary respiratory fluctuation in volume to some degree, at least until sufficient intrapleural pressure exists not only to reduce the tidal exchange of air but also to reduce or obliterate the residual air, and upon relaxation of the counter-pressure of the pneumothorax will re-expand so far as the disease process within the lung will permit. When, therefore, the collapse of a lung or one of its segments is disproportionate to the extent of the apparent pre-existent lesion or re-expansion does not follow abandomment of such collapse) measures (in the absence of evidence of extension of the disease and of a grossly rigid visceral pleura), obstruction of the tributary bronchal tree is to be assumed.

The existence of sufficient contractile tissue within the lung to accomplish relatively complete airlessness is doubtful, without at least balancing or exceeding the atmospheric pressure of air entering the trachea and bronchi plus the suction effect of the respiratory act upon the gaseous content of the lung. Therefore, relatively complete and rapid de-aeration and shrinkage of a lung or its segment upon phrenicectomy, pneumotherax or thoracoplasty cannot be looked upon as a normal reaction. The reduction in volume of a portion of lung which is appreciably greater than

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the actual tissue apparently infiltrated by local disease and exudate (and therefore the site of at least local consolidation) by collapse measures, which do not exceed the sum of the atmospheric pressure plus the force applied by the respiratory action of the thoracic wall and diaphragm, must be an attempt to effect an intrapulmonary gas-pressure balance in the presence of bronchial obstruction to the inrush of air.

We would therefore consider a disproportionate selective collapse, or a spontaneous atelectasis as suggesting the probability of tuberculous bronchitis.

#### SUMMARY

Tuberculous tracheobronchitis exists with sufficient frequency to demand the attention of roentgenologists. Upon examination of serial chest films, the complication may be suggested or indicated to the roentgenologist by any one of the following:

- 1. Atelectasis.
- 2. Spontaneous intermittent atelectasis.
- 3. Extent of roentgen pathology not compatible with clinical course.
- 4. Degree of collapse greater than expected from evident lesion.
- 5. Sudden increased atelectasis with collapse therapy.
  - 6. Visible changes in bronchi.
  - 7. Oechsli's sign.
  - 8. "Tennis ball" cavity.
- 9. Lobular emphysema in a patient with positive sputum.

Although it presents a fairly definite clinical entity, it can be diagnosed during life, with certainty, only by the bronchoscopist.

The assistance of Dr. John B. Barnwell, Associate Professor of Medicine, University of Michigan, in this study is gratefully acknowledged.

#### REFERENCES

- 1. Andrews, C. H. Bronchial stenosis in pulmonary tuberculosis. Canad. M. Ass. J., 1935, 33, 36.
- 2. Ballon, D. H. Bronchoscopy in diagnosis of asthma complicating pulmonary tuberculosis. *J. Thoracic Surg.*, 1935, 5, 103-109.

- 3. BARNWELL, J. B., LITTIG, J., and CULP, J. E. Ulcerative tuberculous tracheobronchitis. Am. Rev. Tuberc., 1937, 36, 8-45.
- 4. Bugher, J. C., Littig, J., and Culp, J. Tuber-culous tracheobronchitis; its pathogenesis. Am. 7. M. Sc., 1937, 193, 515-525.
- 5. Pinner, M. Chapters III and IV in: Alexander, J. The Collapse Therapy of Pulmonary Tuberculosis. Charles C Thomas, Springfield, Ill., 1937.
- 6. Samson, P. C., Barnwell, J., Littig, J., and Bugher, J. C. Tuberculous tracheobronchitis. J. Am. M. Ass., 1937, 108, 1850-1855.
- SPROULL, J. Collapse of the lung occurring in pulmonary tuberculosis. Am. J. ROENTGENOL. & RAD. THERAPY, 1928, 20, 419-423.

#### DISCUSSION

DR. CHARLES R. AUSTRIAN, Baltimore, Md. It is a pleasure to be invited to discuss so clear a presentation of a timely topic as you have just listened to. However, at the same time it is difficult to discuss it because Dr. Peirce and Dr. Curtzwiler have been so complete in the context of their communication. Perhaps I can serve my purpose best by re-emphasizing some of the points and making a few additional ones.

I do not wish to be trite but I think that you will be impressed with the fact that a review of the symptoms emphasizes what has been said before, that all that wheezes is not asthma. It is time that the term asthma be limited more and more to the hypersensitive patient who has the symptom of dyspnea, paroxysmal in type, wheezing, rhonchi, and a paroxysmal cough. There is one point about the dyspnea that patients with tracheobronchial obstruction present which should be reiterated, and that is that quite frequently the patient is objectively extremely short of breath but subjectively seems to mind that shortness of breath very little.

A second point is that not infrequently the symptoms from which he suffers are augmented appreciably by a change in position.

A third point is the extreme variability of the symptoms from time to time regardless of surrounding conditions.

The real contribution, in the main, it seems to me, that the roentgenologist and the roentgenographic study of these individuals gives, is the demonstration of a hindrance to the ebb and flow of air, the normal ebb and flow through the airway. If, as has been indicated so well by the presentation of these patients, there is an appreciable obstruction to the flow of air through the lobar or major bronchi, varying degrees of deficiency of aeration of the lung will result.

This enables us by means of the film to determine that there is insufficient aeration of a .segment or of the entire lung and to suspect that there must be something in the tube which leads the air to the parenchyma to hinder the ingress or the egress, or both, of air. If that hindrance is complete, one gets more or less complete so-called atelectasis (I will not be a purist this morning) of the segment supplied. If there is a complete hindrance of air through the lobar bronchus of a normal lung, one should get more or less complete collapse of the segment interfered with, but if, as Van Allen pointed out, the hindrance is to aeration through a bronchus smaller than a lobar bronchus under ordinary conditions, so-called collateral breathing prevents the development of such collapse.

However, in a disease such as pulmonary tuberculosis where even though the parenchymal change may be relatively slight, such collateral breathing may be interfered with and it is possible, therefore, under these conditions to get pulmonary collapse even though an obstruction occurs in a bronchus smaller than a lobar one. Whether or not that can lead to lobular atelectasis I think is a point that is still moot. The classical manifestations of atelectasis of the lung or of a lobe are so well known that reference to them is unnecessary.

In these instances fluoroscopy is often helpful to confirm one's judgment that it is atelectasis and not consolidation with which one deals, although he may feel that is true because of the diminished volume as evidenced by the film, because of the fact that during inspiration, the dislocation of the mediastinum toward the affected side will be increased, whereas during expiration, or forced expiration, the reverse will be true.

But not all patients who have bronchial or tracheobronchial obstruction have complete obstruction, and quite frequently, as has been indicated, there is obstruction that varies from time to time. One of the signs helpful in the diagnosis of such a state as this is the extreme and rapid variability of the manifestations of hindrance, as evidenced by the roentgenographic changes, by the symptoms and by the sudden disappearance of tubercle bacilli from the sputum, where there has been no concomitant improvement to lead one to suspect an anatomical cause for that change.

If there is valvular hindrance so that the ingress of air is relatively free as contrasted with

the egress of air, then one may get the opposite of collapse, namely, hyperinflation or emphysema, posely called. It is really hyperinflation of the segment aerated by that bronchus. Now and again, in patients with the symptoms and with the manifestations that have been described so well, one gets instead of collapse, hyperinflation and must be prepared to utilize that finding as a corroborative bit of evidence.

The type of cavity to which reference has been made is, I think, considered by all those who have been studying the condition a most useful one, and I wish to add only one statement to that made by Dr. Peirce, that the presence of a spherical or spheroid cavity with thin walls, with or without a fluid level that fails to collapse when collapse therapy is induced, is diagnostically of maximum importance, provided there are no demonstrable adhesions that may have prevented the collapse of the cavity that would otherwise have gone down without obstruction to the bronchus.

The value of knowing the paradoxical effects, if you please, of induced pneumothorax and similar types of collapse therapy on lungs that are tuberculous when there is obstruction has been brought out quite clearly and is of great importance. If all patients who had tracheobronchial tuberculosis had either complete, varying, or valvuar obstruction, our problem would be a little simpler but unfortunately, there is a group in which this type of disease, this localization of tuberculosis causes no appreciable hindrance of the inflow or outflow of air and therefore offers a real difficulty.

Hopkins, at the meeting of the National Tuberculosis Association in Los Angeles in June, pointed out in a series of some five hundred-odd patients with pulmonary tuberculosis, that bronchoscopic examination has shown the presence of bronchial lesions in a little over 30 per cent. Of these, 6 per cent showed roughly no evidence of obstruction at all and therefore in this group, one would be deprived, by roentgenography at least, of the evidence either of collapse or of hyperinffation, and would have to take recourse primarily to one other valuable contribution of the film, namely, as has been pointed out, the great cascrepancy between the symptoms, the physical signs and what was depicted on the film of he chest.

Finally, there is another variety, the type in which only the very small bronchi seem to be involved, the so-called bronchiolar type, or in the smaller branches before the bronchioles

are given off, in which one may have extreme dyspnea, moderate cyanosis, large quantities of sputum rich in tubercle bacilli without any demonstrable diagnostic evidence on the film which presents an appearance not unlike that seen in many cases of bronchiectasis.

I cannot help feeling that what the roentgen ray shows oftentimes in patients with this syndrome is very like what a certain type of artist attempted to depict by his technique in the advertisements with which we were so familiar in the last decade, where, with a minimum of line, to the receptive mind a maximum of suggestion was given. It is the regativity rather than the positiveness of the film that in given cases usually furnishes most of the evidence.

No reference has been made to bronchography and I think perhaps happily, although it has been utilized in a number of these patients by different observers, not without a certain amount of hazard, I feel. However, it has been employed and in a number of instances it has been reported that the defirite presence of obstruction, and its localization has been made manifest in this way. Personally, I have had no experience with it in these patients and would hesitate, I think, to employ it.

Finally, I would say, in epitome, that symptoms lead to a suspicion of the existence of tracheobronchial tuberculosis and the roentgen ray makes the presumpt on extremely strong provided, of course, one has excluded or can exclude other causes of bronchial obstruction. Thirdly, it is by means of the examination of the sputum and with the bronchoscope that the presumption may be proved to be true and the localization of the lesion determined.

Dr. T. A. Groover. Washington, D. C. I would like very briefly to report one case that throws a rather interesting sidelight on this question of tracheobronchitis. About three years ago, a child about six years old was brought to us who for some weeks previously had had wheezing respiration. We made a roentgen examination of this child and found an obstructive emphysema on the right side. There was nothing else significant in the examination other than this obstructive emphysema. We naturally, and I think quite properly, made a diagnosis of non-opaque foreign body and the patient was referred to Dr. Jackson in Philadelphia for its removal. A few days later we got a report from Dr. Jackson that he had removed a grain of puffed wheat from the right bronchus and congratulated ourselves on the diagnosis which we had made. A short time after that, we got a communication, stating that on further examination of this material, removed from the bronchus, they found it to be a tuberculous mass of tissue and this was later confirmed by animal inoculation.

Subsequent to that, the child did develop pulmonary infiltration, in the region of the right hilum which roentgenologically had the appearance of tuberculosis. This ultimately cleared up and the child now is apparently well.

DR. JOHN SPROULL, Haverhill, Mass. Prior to 1928, there were no reports in the English literature regarding collapse of the lung in adult pulmonary tuberculosis. In 1928, in the American Journal of Roentgenology and Radium Therapy, I reported 4 cases of collapse of the lung as a complication of adult pulmonary tuberculosis, and one of these cases was bronchoscoped. At that time, bronchoscopy was not often carried out in tuberculosis and I had some difficulty in getting a bronchoscopist to bronchoscope the patient.

Prior to that time, in such cases the shift of the heart to the affected side had been regarded as the result of fibrosis or previous pleurisy. I had a patient at that time who showed a sputum positive for tuberculosis and who also showed collapse of the lower lobe of the right lung. I was able to observe her every two or three days until she also developed collapse of the upper lobe of the same lung. I was rather interested to know the cause of the collapse and so had bronchoscopy performed.

The bronchoscopy recorded by Dr. Richards of the Peter Bent Brigham Hospital in Boston showed inflammatory edema of the bronchus, and there was some question at that time as to whether the bronchostenosis was the result of external pressure from enlarged glands or whether it was the result of inflammation of the mucous membrane of the right main bronchus.

I communicated with the late Dr. Manges of Philadelphia at that time and he said he had never seen collapse of the lung as a complication of adult pulmonary tuberculosis. He had seen it in childhood due to glandular pressure. It is only fair to state that I did not recognize the pathologic condition as tuberculous bronchitis, but the films were similar to those of the cases here presented by Dr. Peirce which showed complete collapse of one lung.

Since that time, in attending seminars at the

Massachusetts General Hospital and in private practice, I have seen many cases of collapse of the lung in pulmonary tuberculosis, and bronchoscopic examination has revealed in many cases obstruction of a bronchus from granulation tissue. I do not know of any cases wherein opaque bodies such as Dr. Hopkins spoke about have been demonstrated in the bronchi. It is well known that inflammatory edema and granulation tissue in a bronchus occurring as the result of tuberculosis can produce a roentgen picture similar to an obstructing foreign body in the bronchus.

Dr. George E. Pfahler, Philadelphia. I would like to ask whether in any of these cases roentgen treatment has been utilized. It does seem that with the granulation tissue which has just been described, located in these bronchi, as the cause of the obstruction, a moderate amount of irradiation might be helpful.

Dr. Sproull: I might say something on that. I suggested that it might be if these were due to glandular enlargement, but in the cases that I saw and in which I tried it, it did no good.

Dr. Peirce (closing). I wish to thank Dr. Austrian very much for the generous discussion of our paper, and his kind comments.

I apologize to Dr. Sproull for not having found his previous report. It commonly has been my good fortune, each time I say something here, to discover that it was said much better by someone else a long time before.

In regard to Dr. Pfahler's question, roentgen therapy has been tried. If Dr. Jacox is here, I wish he would discuss it. We thought that perhaps it might be of some benefit but I think I can say very definitely and frankly that it is not, and in some cases it has seemed to make the patients worse. I do not believe that irradiation has much to offer these patients. It may possibly in the hyperplastic cases; the type in which, as Dr. Sproull mentioned, there is edema in the early phase before formation of

gross tubercles and before ulceration. But I am extremely disappointed in the results that we have obtained so far with irradiation. In fact, we are so disappointed in it that we feel at the present time the results warrant simply some mention with the statement that it has not had important beneficial effect.

I appreciate Dr. Groover's comment and the description of his very interesting case. The formation of tuberculoma in these individuals seems to be quite common, and I anticipate that is what that was.

Dr. GROOVER: Yes.

Dr. Peirce: I am glad that Dr. Austrian brought out the matter of obstructive emphysema. Dr. Farnwell and I have had considerable correspondence and discussion about it this summer, for it had been called to our attention. Recently, Dr. Barnwell wrote me that he had received, from some of the men who had been kind enough to send in cases for us to see, some films which showed this obstructive emphysema. We had not seen it in our series, or if we had, we passed it over: we have not been aware of it. I think it is another of these important suggestive signs. Dr. Austrian has emphasized the roentgen evidence. The clinical exicence oftentimes develops the suspicion and the roentgen evidence permits the presumption on the basis of discrepancy between the roemtgen signs and the clinical signs or symptoms.

We have found that we were not examining our patients early enough after the induction of pneumothoras. Every such patient has a fluoroscopic examination, but we were not recording the situation on films. Another part of the problem that Dr. Barnwell is now working on is the comparison of inspiratory and expiratory films at the same sitting. These may give additional information. We hope to have some further report, and I anticipate that will come from Dr. Barnwell shortly.



## ROENTGEN ASPECTS OF THE UPPER RETRO-ESOPHAGEAL PULMONARY BORDERS\*

By HERBERT C. MAIER, M.D., Med. Sc.D. NEW YORK, NEW YORK

**Y**N THE upper portion of the thorax posterior to the esophagus the right and left pleural spaces closely approach one another under normal conditions. An appreciation of this anatomical fact is of importance in the interpretation of roentgenograms because the pulmonary borders in this region are sometimes outlined roentgenographically. Various physiological and pathological conditions may displace the medial pleural margins and cause difficulty in the identification of roentgen shadows. It is a rather common misconception that the pleural cavities are separated by a broad mediastinal septum posteriorly in contrast to the almost midline reflections of the mediastinal pleura anteriorly. This erroneous impression is strengthened by published cross-sectional diagrams of the thorax in anatomical treatises which often fail to show the true extent to which the pleural cavities protrude medially in some reg ons of the posterior part of the mediastinum. In the cadaver normal relationships may be distorted somewhat during the process of embalming unless special precautions are observed. Ordinary roentgenograms of the chest representing posteroanterior projections as a rule afford little opportunity to observe the mediastinal pleural relationships.

Heiss<sup>4</sup> studied the posterior pleural borders in the cadaver after the injection into the pleural cavity of a colored fluid mixture which would soldify. He then removed the vertebrae and adjacent portions of the ribs from a posterior approach and thus exposed the posterior part of the mediastinum. He demonstrated that above the level of the aortic arch and the arch of the vena azygos the pleural borders of

the two hemithoraces are close together in front of the vertebral bodies and posterior to the esophagus. The mediastinal pleura of the right side especially lies very close to the median line at this site. The arch of the vena azygos interrupts the medial extension of the right pleural reflection at the level of the fifth thoracic vertebra. Again caudal to the arch of the vena azygos and extending to the level of the tenth thoracic vertebra there is a considerable extension of the right pleural cavity. towards the left side in front of the vena azygos and thoracic duct and posterior to the esophagus. These right mediastinal pleural reflections overlap most of the thoracic esophagus when viewed from

Danelius<sup>2</sup> applied a radiopaque substance to the parietal pleura in cadavers and compared the pleural lines so demonstrated with the shadows seen on the normal posteroanterior roentgenogram. He showed that as one traces the pleural borders of the pulmonary apex medially and downward, it extends on each side far into the vertebral shadow until at the approximate level of the fourth thoracic vertebra the pleurae of the two hemithoraces are almost in contact. This site of close proximity of the right and left mediastinal pleurae was in the upper posterior portion of the mediastinum in front of the vertebrae and posterior to the esophagus. Danelius also pointed out that because of this anatomical fact a portion of lung is projected upon the mediastinal density and is not to be seen in posteroanterior roentgenograms.

In a later paper Danelius<sup>3</sup> reported some clinical roentgenographic studies. By outlining the esophagus with barium, and by

<sup>\*</sup> From the Department of Surgery, University of Michigan, Ann Arbor, Michigan. This work has been aided by a grant from the James and Elizabeth Inglis Fund for Thoracic Surgery.

the use of lateral roentgenograms he came to the following conclusions: (1) A retroesophageal space, that is, a space between the vertebral bodies and the esophagus which contains lung, can be demonstrated in the upper mediastinal region in most subjects. The space may be absent if the curve of the thoracic spine is slight. (2) The retro-esophageal space is larger during inspiration and smaller during expiration. The esophagus follows the trachea closely and moves forward during inspiration, thus increasing the distance between esophagus and vertebrae. (3) The retro-esophageal space is slightly smaller with the patient supine than in the erect position. Even with the patient recumbent, however, in · most instances the esophagus does not rest directly on the vertebral column in this region.

The medial pulmonary borders in the upper posterior portion of the thorax cannot usually be visualized roentgenographically in routine posteroanterior projections because the aerated tissues are insufficient in amount to produce visible contrast. In

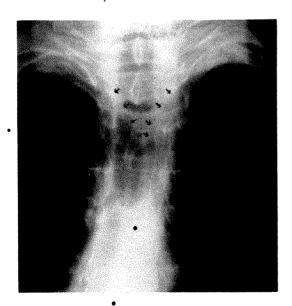


Fig. 1. Arrows indicate pulmonary borders in retroesophageal space superimposed on tracheal outline. Mediastinal pleural borders posteriorly can be seen as continuation of pulmonary apex. At fourth thoracic vertebra pleurae of two sides are almost in contact behind the esophagus.

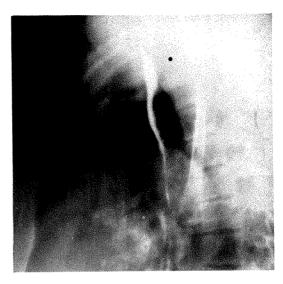


Fig. 2. Lateral regulagenogram with esophagus outlined with barkin. Note retro-esophageal space contains pulmodary tissue above aortic arch.

denser roentgenograms produced with the aid of the Potter-Bucky diaphragm these pulmonary borders can sometimes be observed.

If the mediastinal septum has not been displaced as the result of disease, the pleural borders in the posterior portion of the upper medzaszinum are seen, if at all, as curved marging of aerated lung approximating each other close to the midline of the spine.1 In instances in which the retroesophageal progression of the lung can be visualized roen-genographically it will be seen to be a continuation of the medial pulmonary borders as the outline of the apical portion of the lung is traced medially and downwards into the mediastinal densities. These margins are usually superimposed on the area of diminished density which represents the air column within the trachea (Fig. 1). Between the level of the third and fifth thoracic vertebrae the pleural borders rormally overlap the vertebral column. The point of closest approximation between right and left lungs posteriorly occurs at the level of the fourth thoracic vertebra. The medial extension of the lungs posteriorly is limited below by the arch of the vema azvgos on the right and the aortic arch on the left. Pulmonary

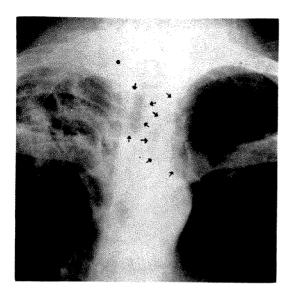


Fig. 3. Arrows indicate margins of retro-esophageal portion of lungs in case of right apical pulmonary tuberculosis associated with emphysema.

tissue in the retro-esophageal space is seen to best advantage roentgenographically in lateral projection (Fig. 2).

The distance between the upper esophagus and the anterior vertebral surface is increased in subjects with thoracic kyphosis, and consequently the retro-esophageal space contains an abnormally large volume of pulmonary tissue. This fact can best be shown roentgenographically in lateral projections when the esopragus is outlined with ingested opaque material. If thoracic kyphosis is associated with emphysema of the pulmonary apices, conditions are most favorable for roentgenographic demonstration of the medial pleural borders in the upper posterior thorax. Occasionally under such circumstances the adjacent margins of lung may be identified in the routine frontal projections without the aid of the Potter-Bucky diaphragm (Fig. 3).

Since the mediastinal pleurae of the two hemithoraces are separated from one another by nothing more than a thin wall of areolar tissue in the retro-esophageal space, it is not surprising that this septum should be rather easily displaced to one side as the result of various pathological conditions within the chest. In a previous communi-

cation<sup>5</sup> it has been pointed out that mediastinal herniation may occur at this site when intrapleural pressures on the right. and left side are unequal. Scar tissue contracture occurring in one pulmonary apex only, or more predominantly in one apex than the other, may cause traction on the mediastinal pleural septum resulting in its displacement across the midline. Under these conditions pulmonary displacement is associated with tracheal and esophageal shift in the same direction. This set of circumstances may produce mediastinal herniation. However, inequality in the intrapleural pressures of the opposing hemithoraces is undoubtedly a much more common cause. Upper posterior mediastinal herniation is encountered occasionally. in patients with pulmonary tuberculosis (Fig. 4). In such an instance the herniated portion of lung may be incorrectly interpreted as representing a pulmonary cavity or emphysematous bulla of the other lung.

After the surgical removal of one lung numerous intrathoracic anatomical readjustments occur. Among those following left pneumonectomy, Rienhoff<sup>6</sup> describes the invagination of the posterior mediastinum by a lappet of the right lung in front of the bodies of the vertebrae but behind the esophagus. A part of the protrusion is above the arch of the azygos vein in the

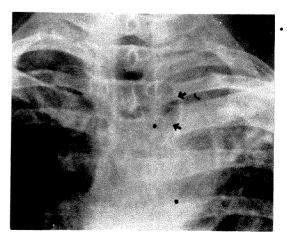


Fig. 4. Arrows indicate border of right lung which has herniated through retro-esophageal space secondary to fibrotic tuberculous process in left apex.

condition, a fall of temperature and a rapid cure. In some cases there occurs a temperature elevation following the irradiation but this is of short duration. In a third group of cases the curative effect of the irradiation is not as striking as in the first two groups and the temperature falls by lysis while the local and general symptoms decrease and eventually disappear in the course of a few days.

The author also employed this type of radiation in the treatment of 60 cases of thrombophlebitis. In not a single case did an embolism occur. The results obtained in these cases were very satisfactory and better than those obtained by any other method of treatment hitherto employed by the author.—A. S. Schwartzman.

HAMANN, A., and GÖBEL, A. Sechsjahresergebnisse bei der Behandlung der Gebärmutterkrebse im Allgemeinen Krankenhaus St. Georg zu Hamburg. (Results of the treatment of carcinoma of the uterus in the course of six years in the General Hospital of St. George of Hamburg.) Strahlentherapie, 1938, 62, 251-261.

In a previous communication these authors reported the results obtained by them from the treatment of carcinoma of the uterus where the patients were under observation from two to four and one-half years. The present report is based on a followup observation of the same cases up to six to eight and one-half years. The present report is based on a study of the pure radiation effect on carcinoma of the cervix. Some studies were carried out also regarding the effect of roentgen radiation on carcinoma of the body of the uterus and these results are compared with those obtained from purely surgical and surgical-radiation treatment of carcinoma of the cervix and of the body of the uterus.

Carcinoma of the Cervix. On December 31, 1933, of the 203 patients with carcinoma of the cervix treated by irradiation alone, 51 remained alive and free of symptoms. On December 31, 1937, 37 of these were alive and free of symptoms, 5 were free of symptoms but died from •intercurrent disease four years after the treatment and 9 died from carcinoma.

Most deaths occurred during the first one and a half years after treatment was instituted. After one year only about 54 per cent of the patients remained alive, after one and a half years only 40 per cent remained alive. During the following one and a half years, that is at the end of the third year, only about 27 per cent remained alive and during the following three years, that is at the end of the sixth year of treatment, only 20 per cent remained alive. Of the 203 cases treated, 44, or 21.7 per cent, lived longer than five years and 41, or 20 per cent, lived at least six years. A study of the cases in regard to the stages of carcinoma at which treatment was instituted showed that 40.7 per cent of these remaining alive after six vears and free of symptoms were those who came to treatment while in Stage 1.

No essential difference was found in regard to the age of the patients. The results, however, were somewhat better in younger than in middle-aged womer. Below sixty years of age the earlier results were definitely more favorable. After six years of observation 22 per cent of those remaining alive were between twentyone and forty year: of age, 17 per cent were between forty-one and sixty years of age and 20 per cent above sixty-one years. If we further consider the mortality resulting from intercurrent infections the results in the last mentioned group appear even more favorable.

Carcinoma of the Body of the Uterus. Of the 13 patients with carrinoma of the body of the uterus of Stages \* tc IV, 4 were alive and free of symptoms on December 31, 1933. Two of these remained free cf tumors. In 2, recurrences appeared during the sixth year, in one in the lesser pelvis and in the other in the vulva and in the inguinal regions. The last mentioned 2 patients were still a ive seven years after the treatment of the primary tumor.

Recurrences. Of 32 cases of surgical recurrences, 33 cases of carcinoma of the pelvis and 2 cases of carcinorna of the body of the uterus, 7 remained alive on December 31, 1933, 2 of which were the two vomen with carcinoma of the body of the uterus. These 2 patients remained alive and free of symptoms on December 31, 1937. Of the remaining 5 cases 2 died, one from intercurrent infections and the other from another recurrence.

Results obtained from the surgical and radiation treatment of carcinoma of the uterus:

1. Carcinoma of the Cervix. Of 58 operative cases 46 of which were later treated with roentgen rays, 27 remained free of symptoms on December 31, 1933. Since then 3 cases died, 1 from pulmonary tuberculosis during the sixth year after the operation and 2 from carcinoma three and six years after the operation respectively; 26 of the 58 cases remained alive and free of symptoms five years after the operation and 44 of the 58 remained alive and free of symptoms six years after the operation.

Of the 20 cases operated on at another clinic but treated in the present clinic by roentgen irradiation, 8 remained free of symptoms on December 31, 1937. The results obtained from the combined surgical and radiation treatment were: Free of symptoms and alive 42.4 per cent after five years and 39.8 per cent after six years following surgery and roentgen treatment.

2. Carcinoma of the Body of the Uterus. Fifty per cent of the 14 cases treated remained alive and free of symptoms five and six years after the operation. One patient died from carcinoma two years after the operation.—A. S. Schwarzman.

#### MISCELI AMEOUS

STAUNIG, K., and I ÖBERING, J. Über einen neuen Röntgeneffekt. (A new roentgen effect.) Strahlentherapie, 1938, 62, 73-90.

Roentgen rays have a definite effect on the atomic structure of tissue. It is conceivable that this effect is not limited to the atom alone. In consideration of the above the authors studied the effect of roentgen rays on the swelling ability of various tissues; they have found that this ability to swell undergoes a change when the tissue has previously been acted on by roentgen rays. Depending on the tissue used. it was found that under the influence of roentgen irradiation the degree of swelling is either increased or decreased. In the experiments carried out hitherto it was found that in many instances the ability of the tissue to swell increased following the irradiation by 3.6 per cent above normal while in other cases the same ability was decreased by 1.4 or more per cent. The structure of the tissue apparently influences this change considerably. Changes in the swelling ability were observed in bone marrow, cartilage, lung tissue, testicular tissue, ovarian tissue, striated muscle, thyroid tissue and pancreas. Extensive studies have shown that the presence of the biological cell is unnecessary for the appearance of the above mentioned changes and that the effect appears in the absence of biological cells in a similar manner. Apparently other properties of the substance which must be looked for in the chemico-physical structure are responsible for the changes resulting under the influence of

roentgen irradiation. It was found, for instance. that the same changes in the swelling ability occur in gelatin as in cartilage and in numerous other animal tissues. These findings would indicate that in the evaluation of the roentgen effect the molecule of the tissue irradiated is of significance. Under certain conditions the molecule is capable of changes when the roentgen rays are acting on it. The changes in the molecule come to manifestation in the form of changes in its external valences. The biological effect of roentgen rays is basically the result of the fact that the vital manifestations are dependent on changes taking place in the colloidal condition. These data are of great value for roentgen therapy.—A. S. Schwartzman.

Laszlo, D., and Fleischmann, W. Strahlenwirkung auf den Zellstoffwechsel. (Effect of radiation on the cellular metabolism.) *Strahlentherapie*, 1938, 62, 151–155.

Many problems pertaining to the biological effect of radiation still remain unclear. One of these problems is the latent time. If, for instance, a cellular culture is irradiated with 120 mg-hr. of radium, this dose does not suppress the cellular growth immediately. According to the computation of Lischer, about 15 g. of radium is necessary in order to produce an immediate cessation of growth and an immediate cellular death. The duration of the latent time is constant with constant radiation doses and is independent of the proliferation size of the cell. With increasing radiation intensity the duration of the latent time is shortened. Canti and Spear have found that the mitoses disappear rapidly after irradiation with small doses. According to Fischer the cessation in growth following the irradiation can not be explained by the fact that only the cells in a state of mitosis are affected by the rays. If this were correct one could expect an immediate effect of the irradiation. His experiments may be interpreted only in the sense that all cells are uniformly affected by the rays. He is of the opinion that the irradiated cells liberate growth inhibiting substances which gradually lead to a cessation of growth of the culture. Heeren studied extensively the latent time of the radiation effect and expressed the opinion that the time interval of the latent period will be considerably shortened with a further improvement of our methods of study. The question arises whether the inhibition of growth is the result of an inhibition of the energy metaboregion under discussion in this paper. The roentgenological appearance of the protruding portion of lung in the upper posterior portion of the mediastinum after pneumonectomy is seen in Figure 5. This roentgenogram was obtained several months after complete removal of the left lung because of a bronchial tumor associated with cystic destruction of the entire lung.

Although several instances of mediastinal herniation through the weak place in the upper posterior portion of the mediastinum have been observed in our clinic. these have all been in the same direction from right to left. We have never encountered an instance of herniation at this site in which the lung protruded into the right hemithorax. It may be that the aortic arch acts as a partial barrier against bulging toward the right since just below this region the aorta itself protrudes slightly towards the left and may limit the shift of the lung and mediastinum toward the right. Under normal circumstances the posterior mediastinal pleura on the right lies closer to the midline than does the pleura on the left.

Sometimes when seen in roentgenograms the posterior pulmonary borders are thought to represent the medial margins of lung anteriorly. In several published articles this erroneous assumption appears to have been made. Since the only point of close approximation between right and left lungs above the upper margin of the manubrium occurs posteriorly, it is obvious that when medial pulmonary margins can be made out close to the midline above the manubrium they must represent relationships in the posterior mediastinum. Except under most unusual circumstances the pleural borders do not approach the midline anteriorly above the superior margin of the manubrium. A clear understanding of these relationships is of advantage in differentiating anterior and posterior pulmonary borders as seen roentgenographically. Lateral shifting of visible pulmonary margins in relation to trachea or esophagus

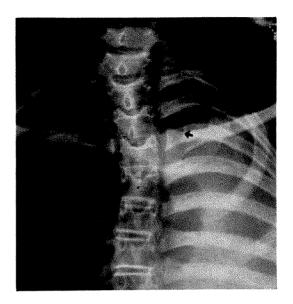


Fig. 5. Roemtgenogram obtained several months after left total pneumonectomy. Arrows indicate border of right lung which has protruded posterior to trachea and esophagus into left hemithorax. The outline of the anterior mediastinal hernia can be seen below the sternoclavicular level.

with various degrees of rotation about the vertical axis of the thorax serves to verify the relatively anterior or posterior position of visible pulmonary margins near the midline.

There is usually no difficulty in differentiating these pleural borders from the tracheal outline. The band of diminished density which represents the air column within the trachea can be traced upward into the cervical region and usually stands out rather clearly against the background of surrounding structures of greater density. The trachea is rarely as sharply curved at any point in its course as the pulmonary margins in this region may be. Furthermore, the pleural margins can usually be traced as a medial continuation of the pulmonary borders in the thoracic apex.

It is apparent when one studies the relationships of the pleura in the upper posterior portion of the mediastinum that an appreciable amount of pulmonary tissue in this mangin may be hidden from view in the roentgenograms prepared in the usual



Fig. 6. Right upper thoracoplasty without apicolysis performed for pulmonary tuberculosis. Arrows indicate border of retro-esophageal portion of right lung.

posteroanterior projection. Obvious lesions localized to these medial portions of lung may easily escape notice even on otherwise adequate roentgen examination. No information is available as to the frequency with which lesions restricted to lung in this position occur. Cases of pulmonary tuberculosis have been observed, however, in which following thoracoplasty without apicolysis an appreciable amount of uncollapsed lung was present in the upper retroesophageal space (Fig. 6). In a few such instances this was an important factor in

inadequate surgical collapse of the tuberculous portion of the lung.

#### SUMMARY

- 1. The mediastinal pleurae of the two hemithoraces are in close proximity in a part of the upper posterior portion of the mediastinum between the esophagus and vertebrae.
- 2. The displacement of these pleural borders by various physiological and pathological processes is described.
- 3. The roentgenological interpretation of these pulmonary borders is discussed.

#### REFERENCES

- BÁRSONY, T., and WALD, B. Das Röntgenbild der oberen-hinteren schwachen Stelle des Mediastinums. Der prävertebrale, retroösophageale Lungenteil. Röntgenpraxis, 1936, 8, 88-95.
- DANELIUS, G. Experimentelles über den Verlauf der oberen Lungengrenze im Röntgenbilde. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1929, 40, 249-261.
- 3. Danelius, G. Röntgenologie der oberen medialen Lungenabschnitte. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1931, 44, 626-634.
- 4. Heiss, R. Über die hinteren Pleuragrenzen. Arch. f. Anat. u. Physiol., Anat. Abt., 1919, 130-136.
- 5. Maier, H. C. Mediastinal hernia in the absence of pneumothorax. Am. J. Roentgenol. & Rad. Therapy, 1938, 39, 687-697.
- 6. RIENHOFF, W. F., Jr. Intrathoracic anatomical readjustments following complete ablation of one lung. J. Thoracic Surg., 1937, 6, 254-277.



## AN ANATOMICAL, PATHOLOGICAL AND ROENTGEN-OLOGICAL STUDY OF THE INTERVERTEBRAL JOINTS OF THE LUMBAR SPINE AND OF THE SACROILIAC JOINTS\*

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I. ROENTGENOGRAPHY OF THE LUMBAR SPINE. AN EVALUATION OF THE OBLIQUE VIEW

THE value of the oblique projection of THE value of the oblique product the lumbar spine, known as the "Dittmar position" in European literature, was indicated by Meyer-Burgdorff<sup>25</sup> in his monograph on spondylolisthesis and by Hubeny19 in this country in 1931. Since then, Ghormley and Kirklin, 13 Ghormley, 12 Hadley,15 Morton,27 Oppenheimer32 and others have stressed its importance in the study of changes in the facets and apophyseal (intervertebral) joint spaces of the lumbar spine, the position and structure of the neighboring bone and neural arch, and the relation of the articular processes to the vertebral bodies and intervertebral spaces. Ghormley and Kirklin, and Morton have noted that it is possible to get a new view directly through the upper part of the sacroiliac joint, and suggested that this position might prove of value in the diagnosis of certain sacroiliac diseases. All authors advocate a 45° oblique position, although Ghormley and Kirklin recommended a position with the transverse axis of the pelvis at a 32° angle with the horizontal plane.

Arthritic changes involving the zygapophyseal joints become manifest on the roentgenogram by a loss of the smooth margin of the joint surfaces, diminution in the width of the joint space, and roughening and pointing of the articular processes. These changes, advocated by some (Putti, <sup>33</sup> Ghormley, <sup>12</sup> Oppenheimer<sup>29,30,31</sup>) as a cause of low backache and of the sciatic syn-

drome, have been noted during routine gastrointestinal and urinary tract roentgenographic studies in the absence of any history of local or radiating pain in the back.

Hadley<sup>16,17</sup> has discussed the diagnosis by means of the anteroposterior and 45° oblique views of the lumbar spine, of subluxations of the zygapophyseal joints with bony impingement of the upper end of the superior facet against the pedicle above, or of the lower end of the inferior articular process against the lamina below, and believes that such contact may cause pain in the back. Such subluxations he believes are either secondary to narrowing of the intervertebral disc or to increased lumbar lordosis. Morton has observed that the distance between the tips of the articular processes and adjacent bony structures normally diminishes progressively from above downward in the lumbar spine and lumbosacral area. That such subluxations of the articular facets with narrowing of the intervertebral foramina are more apt to follow exaggeration of the lumbar lordosis or narrowing only of the posterior part of the intervertebral disc as suggested by Ayres,1 Williams, 45 and Williams and Yglesias, 46 is indicated by the following observation: If the entire intervertebral disc between two vertebrae is excised and the adjacent vertebral bodies approximated, the result is a separation of the facets and an enlargement of the interventebral foramina, but if only the posterior portion of the disc is removed or if the lumbar segments are hyperextended, subluxation of the facets with

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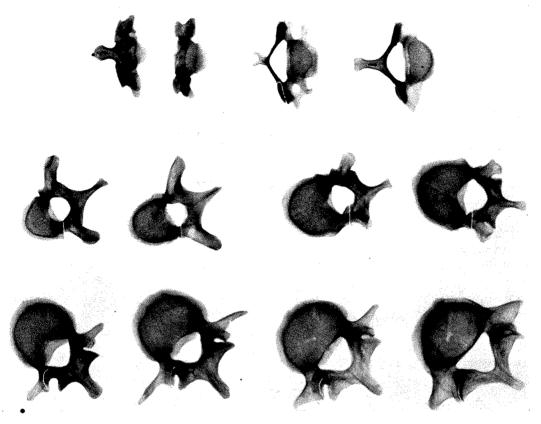


Fig. 1. Upper row (left to right)—2nd, 3rd, 5th and 7th cervical vertebrae. Middle row (left to right)—2nd, 5th, 8th and 12th thoracic vertebrae. Lower row (left to right)—2nd, 3rd, 4th and 5th lumbar vertebrae. The position of each vertebra indicates the position of the patient (the lower border of the figure representing the plane of the roentgen table) for best visualizing the facets and apophyseal joint spaces nearest the roentgen film. The plane of the superior facets of the cervical and thoracic vertebrae is flat; in the lumbar vertebrae it is concave.

constriction of the intervertebral foramina is seen to occur.

In our study, 25 human adult lumbar spines and pelves, all male, were denuded of their overlying soft tissues and were roentgenographed in the anteroposterior, lateral, and right and left 45° oblique planes, and where the transverse process of the fifth lumbar vertebra appeared to impinge on the ala of the sacrum or the ilium, a 45° oblique view of the lumbosacral region was taken from below upwards. These anatomic specimens were studied grossly with reference to changes in the bodies, accessory processes, apophyseal and sacroiliac joints and then sectioned in the midsagittal plane for study of the vertebral bodies, intervertebral discs, the spinal canal and its contents.

Extensive Paget's disease of the bone (osteitis deformans), involving the lumbar spine and pelvis, was noted in the roent-genograms of 2 specimens. The following conclusions were drawn following these comparative anatomical and roentgenological studies:

1. Facets and apophyseal (intervertebral) joints of the lumbar spine whose axes are other than 45° from the sagittal plane may falsely appear the site of pathological processes on the routine 45° oblique views. In 13 of the 25 specimens, although the apophyseal joints were grossly uninvolved, the 45° oblique roentgenogram strongly suggested pathological changes; in all of these specimens the angle of the joint line, measured from the sagittal plane, exceeded or was less than 45 degrees.

- 2. Accessory ossicles (epiphyses) at the tips of the articular facets are frequently not visualized on the roentgenogram, and one may infer that fractures in this region might also remain undiagnosed.
- 3. Degenerative changes in the intervertebral discs are noted on the roentgenogram only after they are advanced and associated with narrowing of the intervertebral space and marginal bony proliferation.

Nuclear herniations into the vertebral body are visualized only when they are surrounded by a zone of osseous sclerosis. Herniations of the intervertebral disc into the vertebral body (Schmorl's cartilage nodes), measuring from 4 to 8 mm. in diameter, were present grossly and evident roentgenographically in 3 instances; they were not visualized on the roentgenogram,

- although present in the gross specimen in 3 other instances.
- 4. Subluxations of the articular facets, as described by Hadley, occur most frequently with narrowing of the posterior part of the intervertebral disc. Apparent subluxations in the presence of intervertebral discs of normal height are due to bony proliferation of the articular margins of the facets.
- 5. The diagnosis of degenerative changes, especially of ankylosis, of the sacroiliac joint, by the roentgenogram, is frequently not corroborated by actual dissections. The 45° oblique projection penetrated directly through the upper part of the joint space in only 6 of 28 normal sacroiliac joints.
- 6. The oblique view of the lumbar spine is valuable in visualizing marginal prolif-

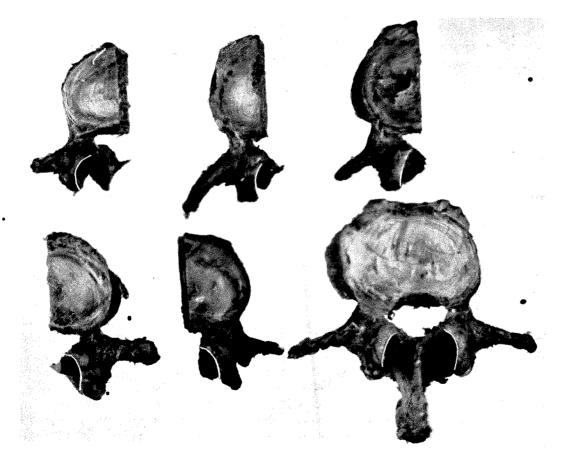


Fig. 2. Superior facets of the third lumbar vertebra. There is variation in the shape of the articular surfaces and in the angle of these surfaces from the sagittal plane of the vertebrae.

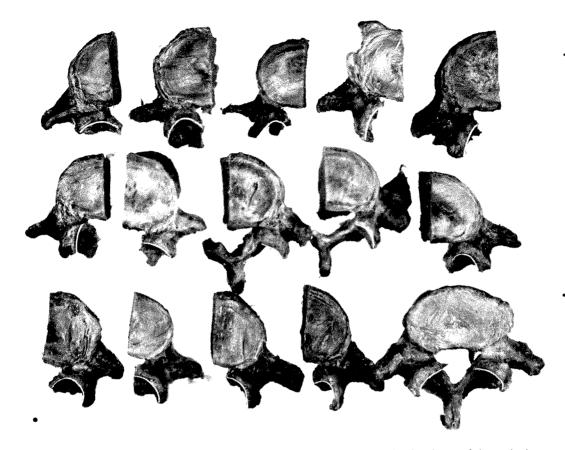


Fig. 3. Superior facets of fourth lumbar vertebra. There is wide variation in the shape of the articular surfaces of the facets, from flat to markedly concave; the angle of the plane of these surfaces varies from the coronal to the sagittal planes.

eration of the vertebral bodies, which is usually most advanced anterolaterally; and it is an additional method in diagnosing impingement of the fifth lumbar transverse process against the sacrum or ilium.

# II, STUDIES OF THE ARTICULAR FACETS AND APOPHYSEAL JOINT SPACES

Since the articular surfaces of the facets of the cervical vertebrae are flat, and are at right angles to the sagittal plane of the body, they are visualized clearly on the direct lateral view roentgenogram of the cervical spine. The facets between the atlas and epistropheus converge so that the inferior facets of the first cervical vertebra look downward and medialward, and are visualized on the anteroposterior view through the open mouth (Fig. 1).

In the thoracic region the articular facets are flat, almost vertical and are placed at an angle of 70° to the horizontal plane. They are roentgenographed with the patient ly; ing in the prone-lateral position on the side of the facets to be studied, the opposite side of the breast being raised to an angle of 70° from the table (Fig. 1).

In the lumbar vertebrae and in the inferior facets of the twelfth dorsal vertebra, the axis of the plane of the facets, which are vertical, is rotated backwards at an angle of 45° so that the superior articular process looks dorsalward and medialward, and the inferior ventralward and lateralward. To visualize them roentgenographically, it is advised that the patient lie in the supine-lateral position, on the side in which the facets are to be roentgenographed, with

the opposite side raised to an angle of 45° from the table (Fig. 1).

In our study, the lumbar and lumbosacral facets and the zygapophyseal joints were investigated in 80 lumbar spines and pelves, 76 male and 4 female, 44 colored and 36 white. An analysis of Table 1 shows that while the lumbosacral facets (5L-1S) are usually flat (85.9 per cent), in 14.1 per cent the superior facet of the first sacral vertebra is concave, and the inferior facet of the fifth

which may falsely give the impression of changes in the clarity and width of the joint space or of increased density of the adjacent bone.

In addition, the zygapophyseal joint space and the surrounding structures will be accurately visualized only if the planes of the articular facets, even if they are flat, are the same or almost the same as that of the oblique projection of the roentgenogram (i.e., 45°). The facets and zygapo-

ANALYSIS OF A STUDY OF THE APOPHYSEAL JOINTS AND ARTICULAR FACETS
IN 80 LUMBAR SPINES AND PRIVES

Articular processes between  No. of lumbar spines dissected		5L-1S	4L-5L	3L-4 <b>L</b>	2L-3L	1L-2L
		80	80	7.3	40	
Angle of axis of apophyseal joint space, as measured from the sagittal plane (figures in percent)	Symmetrical	63.2	78.9	81.7	82.1	80.0
	Asymmetrical	36.8	21.1	18.3	17.9	20.0
	90° 75° 60° 45° 30° 15° 0°	5.0 5.0 26.0 44.0 9.0 6.0 5.0	2.2 1.1 22.2 65.7 4.4 2.2 2.2	3.5 33.3 22.1 20.3	10.9 34.8 30.4 23.9	25.0 50.0 25.0
Shape of articular surfaces (figures in per cent)	Symmetrical	76.3	75.0	78.7	73.1	71.4
	Asymmetrical	23.7	25.0	21.3	26.9	28.6
	Flat	85.9	50.8	19.3	21.2	44 · 4
	Concave-convex	14.1	49.2	80.7	78.8	55.6
Bilateral fusion of apophyseal joints		I	j.		I	I

lumbar vertebra is convex; that the incidence of this latter relation increases in the upper lumbar vertebrae, 49.2 per cent between the fourth and fifth; 80.7 per cent between the third and fourth; 78.8 per cent between the second and third; and 100 per cent between the first and second lumbar vertebrae (Figs. 2–5). This curvature of the articular surfaces, since penetration of the roentgen rays in a plane parallel to the joint surfaces is impossible, will produce on the roentgenogram a summation of shadows

physeal joint spaces between 5L-1S in 56 per cent, between 4L-5L in 34.3 per cent, between 3L-4L in 60.7 per cent, between 2L-3L in 89.1 per cent and between 1L-2L in 100 per cent of our specimens, would not have been accurately visualized by a 45° oblique view of the lumbar spine (Table 1). The true lateral view visualizes those facets and joint spaces in the coronal plane, and the anteroposterior view, those in or almost in the sagittal plane. The possible value of additional 60° and 30° oblique

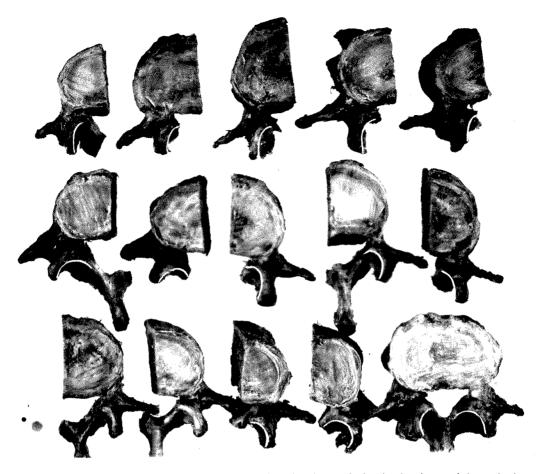


Fig. 4. Superior facets of the fifth lumbar vertebra. There is wide variation in the shape of the articular surfaces and in the angle of these surfaces from the sagittal plane of the vertebrae. There is "tropism" of the superior facets in the complete vertebra illustrated at the right end of the lowest row of specimens.

views of the lumbar spine, when the 45° views are suspicious of pathological change in the facets and their joint spaces, is suggested by the wide variance normally present in the plane of axis of these joints (Figs. 2-5).

Degeneration of the cartilage of the articular processes with marginal bony proliferation and capsular thickening and occasionally ankylosis was present in 31 per cent of the 80 specimens. Such changes were most advanced in the zygapophyseal joints between the third and fourth and between the fourth and fifth lumbar vertebrae and were less marked in the lumbosacral facets, findings which are in keeping with those of Putti and Logroscino<sup>34</sup> in their study of 75 spinal columns.

"Tropism" of the lumbosacral facets, i.e., the plane of the articular processes being coronal on one side and sagittal on the other, was found in 8 specimens and was associated in all with advanced degenerative changes in the adjacent vertebrae, intervertebral joints and cartilaginous discs. Similar advanced changes were found in 7 out of 8 specimens where the facets were bilaterally placed in the sagittal plane. Where the facets were in the more stable coronal plane (7 specimens) such advanced changes were seen in only three.

The posterior margin of the fourth lumbar vertebra extended posterior to that of the fifth lumbar vertebra for a distance of  $\frac{1}{8}$  to  $\frac{1}{4}$  of an inch in 9 specimens, and was associated in each instance with marked

degenerative changes in the lumbosacral intervertebral disc and with marginal bony proliferation. In no instance was a defect noted in the neural arch, accessory processes or vertebral body. In only one instance were the planes of the lumbosacral facets less than 45° from the sagittal plane of the body; a fact at variance with the teachings of Ferguson<sup>10</sup> and others<sup>18,20,22,41</sup> who have discussed the diagnosis of "posterior spondylolisthesis" and its rôle in the etiology of backache.

#### III. ACCESSORY ARTICULAR PROCESSES

These processes are described as instances of ununited accessory epiphyses by a number of authors (Nichols and Shiflett, 28 Fulton and Kalbfleisch, 11 Rendich and Westing 33). Their occurrence is not unusual in the light of the frequency of occurrence of ununited secondary centers of ossification at the tips of the spinous and transverse processes. McMurrich, 24 in describing

the appearance of the vertebral secondary centers of ossification at puberty, notes that "in he lumbar vertebrae, others appear at the tips of the articulating processes." Beiley2 believes that such fissures across the vertical articular process are formed more commonly by the presence of ununited accessory centers of ossification. and are to be differentiated from fractures. Of the 5 cases of "isolated fractures of the articular processes of the lumbar vertebrae" reported by Mitchell,26 3 in which the lesion was kilateral and unassociated with a history of trauma probably represent cases of ununited accessory epiphyses. Bailey collegted 19 cases from the literature, 6 of these bilateral, and added 10 of his own, one bilateral. All involved the inferior articular processes, except one which occurred in the right superior articular process of the third lumbar vertebra.

In our investigation of 100 adult lumbar spines, there were accessory facets, uni-

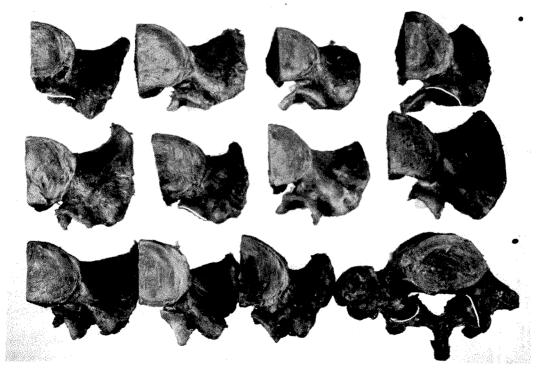


Fig. 5. Superior facets of the first sacral vertebra. There is wide variation in the shape of the articular surfaces and in their angle from the sagittal plane of the vertebrae. There is "trapism" of the inferior facets of the fifth lumbar vertebra illustrated at the right end of the lowest row of specimens.

lateral or bilateral, single or multiple, in 14. The protocols of these specimens were reviewed and in no instance was there a history of severe trauma to the lower spine. In many, a smooth cartilaginous surface lined the opposing fragments, but occasionally only fibrous tissue was found interposed. In 2 of these specimens, there was an anterior displacement of the fifth lumbar vertebra on the sacrum, associated with a bilateral pedicle defect in the fifth lumbar vertebra (anterior spondylolisthesis). The accessory ossicles occurred at the tips of the superior facets in 4 specimens, and involved the tips of the inferior facets in seven (Table II).

Böhmig and Prévot, who in 37 per cent of proved autopsy specimens found no roentgen evidence of intervertebral disc. herniations. Chasin<sup>7</sup> produced artificial defects in the vertebral column, as well as in the bones of the hip and knee joints, in an effort to demonstrate the limitations of roentgenology as a diagnostic measure. Lachmann,23 after studying more than 190 artificially produced defects of varying size and location in the bones of the knee joint, found that conoid shaped excavations involving only the cancellous bone required a diameter of 0.75 to 1.75 cm. at their base and a depth of 0.5 to 2 cm. before they could be visualized on the roentgenogram.

TABLE H

Vertebra Articular facet		Inf.	L.4		L5		ıS
			Sup.	Inf.	Sup.	Inf.	Sup.
Unilateral	Right	1		1	1		1
	Left	ı	1	I		1	
• Bilateral						2	1

There were multiple occurrences of these accessory processes within the same specimen, in 3 lumbar spines:

- L5-inferior facet-bilateral
   L5-superior facet-bilateral
   L4-superior facet-bilateral
- L5-inferior facet-bilateral L5-superior facet-unilateral (left) L4-inferior facet-unilateral (right)
- 3. L5-inferior facet-bilateral L4-inferior facet-unilateral (left) L4-superior facet-bilateral

IV. ROENTGEN DIAGNOSIS OF INTER-VERTEBRAL DISC HERNIATIONS INTO THE VERTEBRAL BODY

Snure and Maner<sup>43</sup> in a study of the roentgen appearance of metastatic malignancy of bone noted that spongiosa occupying an area of 2×2.5×2.75 cm. and 1 cm. deep could be removed and replaced by paraffin, without roentgen evidence of a defect. They call attention to the work of

Wagoner,<sup>44</sup> by immersing vertebrae in water to simulate body tissue opacities, found that a defect in the spongiosa of  $4\times6\times9$  mm. size had properties permitting accurate diagnostic possibilities by the roentgen ray. Similarly, the absence of roentgenographic evidence in certain metastatic malignant lesions of the osteolytic variety in the vertebral column has been noted by Simpson,<sup>40</sup> Kaufmann,<sup>21</sup> Grausman and Sutro,<sup>14</sup> and others, the defect becoming visible only when it is large enough to produce a definite contrasting shadow, or when osteosclerosis occurs in the surrounding tissues.

In our studies two vertebral bodies were sectioned in the sagittal plane and numerous cavities created in the spongiosa, measuring from 2 to 6 mm. in diameter, and these were filled with intervertebral disc material. These specimens were roentgenographed but in no instance could any

defect be definitely visualized (Fig. 6).

Interest in the histologic characteristics of intervertebral disc herniations was initiated by the writings of Schmorl<sup>38</sup> and supplemented by the contributions of Beadle,<sup>3</sup> Calvé and Galland,<sup>6</sup> Sashin,<sup>37</sup> Compere and Keyes,<sup>8</sup> and others. They noted that the nuclear material is extruded through a crack or other defect in the cartilage plate

- 1. State of calcification or trabecular condensation of the surrounding bone.
  - 2. Constent of the defect.
- 3. Relative amounts of cortical and spongy bone overlying the defect.
- 4. Diameter of the transradiated bone which is superimposed over the defect.
- 5. Distance of the defect from the tube and from the film.

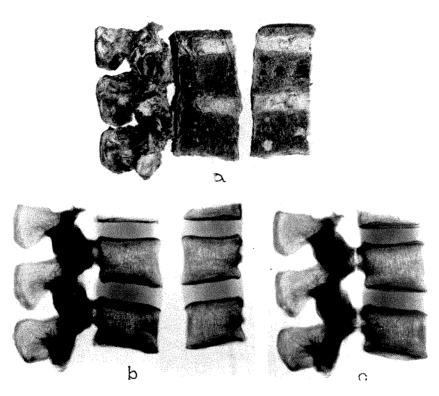


Fig. 6. a, numerous defects, measuring from 2 to 6 mm. in diameter, have been created in the spongiosa of two lumbar vertebrae, and these have been filled with intervertebral disc material (as shown in the lower vertebra). Roentgenograms of both sagittal sections, separately, b, and together, c, fail to visualize any demonstrable defects.

into the spongy bone and becomes transformed into a cartilage nodule. A reaction of the adjacent bone is set up as a secondary line of defense against the invading disc material. It is only after this zone of bony sclerosis and increased calcification appears that the herniation becomes evident roent-genographically.

There are therefore several factors which determine the visibility of a bony defect in the roentgenogram:

6. Direction of the longest axis of the defect in relation to the central roentgenray beam.

### V. ANATOMICAL, PATHOLOGICAL AND ROENT-GENOLOGICAL OBSERVATIONS ON THE SACROLLIAC JOINT

The articular portion of the sacroiliac joint is of the diarmrodial type. Sashin<sup>36</sup> noted the features of a true diarthrodial joint in all human sacroiliac joints up to

the age of thirty (43 subjects). We obtained the same impression from those specimens in our series in which degenerative changes had not yet appeared. We believe that the frequent occurrence of pathological changes in the sacroiliac joint above the age of thirty may explain why some anatomists have described this articulation as an amphiarthrosis. The anterior sacroiliac ligament is relatively weak and is easily torn by distracting the innominate bones after dividing the symphy-

herein recorded, coincide in great part with those made by Testut (Table III).

In the upper part of the articular surface of the sacrum the distance between the anterior margins of the articular surfaces is consistently less than the measurement between the corresponding points on the posterior articular margins. Although a transection of the sacrum in its upper level is shaped like a cone with its base on the ventral (pelvic) side and offers an unstable mechanism against the shearing forces

Table III

MEAN MEASUREMENTS BETWEEN THE SACROILIAC JOINT SURFACES IN 28 SPECIMENS (Extent of variation in parenthesis)

	Anterior	Posterior	
Upper plane of sacroiliac joint	9.93 cm. (8.2-11.1) (11.29 cm. (10.2-11.7) is distance between the joint surfaces just behind the anterior margins)	10.47 cm. (9.0-11.4)	
Middle plane	9.01 cm. (8.1~ 9.9)	9.41 cm. (8.3-10.8)	
Lower plane	9.78 cm. (8.1-10.2)	8.49 cm. (7.5- 9.6)	

sis pubis. The posterior sacroiliac ligaments, consisting of the long, short and interosseous ligaments, and the accessory sacroiliac ligaments (sacrotuberous and sacrospinous) are essential in supporting the sacrum as it lies slung between the iliac bones, bearing the rôle of keystone of an arch and transmitting the weight of the trunk to the lower extremities. Reciprocal sinuosities, tubercles and depressions, permit an interlocking of the articular and nonarticular surfaces. Anteriorly the joint resembles an S, being concave inwards above the innominate line, and concave outwards below this line. Testut,43 disagreeing with most other anatomists, measured 10 sacrums in their superior, middle and inferior planes and concluded that the width between the margins of both sacroiliac articular surfaces dorsally exceeded the corresponding anterior measurements in all planes, especially the middle.

Measurements on 28 macerated sacra,

from above, the sudden deviation of the articular surfaces toward the midline anteriorly, therefore, creates a factor of mechanical safety. Further stability is added by the alternating variations between the ventral (pelvic) and dorsal measurements in the various horizontal planes of the sacroiliac joint, the dorsal measurements exceeding the ventral in a mid-transection, and the ventral exceeding the dorsal measurements in a low transection. In a plane at the lowest portion of the sacroiliac joints the dorsal measurements again exceed the ventral measurements (Fig. 7).

With deficient bony mechanical strength in the upper region of the sacroiliac articulation, where much of the superincumbent weight is transmitted due to the almost horizontal position of the human sacrum, much depends on the posterior sacroiliac ligamentous structures. It is not unusual that pathologic changes should become evident first or advance more rapidly in the

upper portion of the joint. Brooke,<sup>5</sup> in a study of 200 anatomical specimens, found ankylosis of the sacroiliac joint in 37 per cent of 75 male specimens and none in the female specimens. Sashin<sup>36</sup> in 257 fresh and macerated pelves found progressively advancing degenerative changes in the sacroiliac joints above the age of thirty. Bony ankylosis was noted in 57 per cent of male and 5.8 per cent of female sacroiliac joints

seen in 37 specimens, and ankylosis of the sacroiliac joint was present in 21 specimens, all male. As observed, also, by Schunke,<sup>39</sup> changes were noted first, or were found more advanced in the posterior portion of the anterosuperior part of the capsule and anterior sacroiliac ligaments, with exostosis formation followed by complete bony bridging (Fig. 8). In the more advanced specimens this bony ankylosis

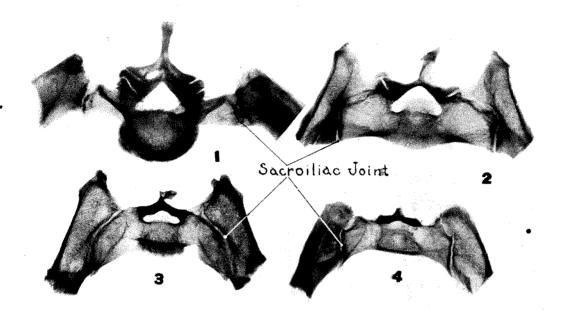


Fig. 7. Transections through the sacroiliac joints in the upper 1, middle 2, and lower 4, planes and in a plane, 3, midway between 2 and 4. The regularity and the direction of the plane of the joint cavities vary widely in these different levels. A 45° oblique roentgenogram would have clearly visualized only the uppermost portions of these articulations.

between the ages of thirty and fifty-nine, and in 82 per cent of male and 30 per cent of female sacroiliac joints above the age of sixty. Schunke<sup>39</sup> noted that partial bony ankylosis of the sacroiliac joint was common after the fifth decade, especially in males, and found extra-articular ankylosis in 9 out of 21 adult bodies, bilaterally in seven.

This study comprises an analysis of 100 human pelves (200 sacroiliac joints) of which 94 were male, 6 female, 54 black and 46 white. Degenerative changes, consisting of fibrillation of the articular cartilage and marginal bony proliferation, were

extended downwards, invading the joint cavity until complete fusion of the joint surfaces was present. The frequent occurrence of extra-articular ossification superiorly, or synostosis of the superior portion of the sacroiliac joint, with the remaining portions of the joint intact, was a striking observation. Ankylosis of the entire articulation was present in 16 specimens and partial ankylosis in 15, a total occurrence of 31 ankylosed sacroiliac joints (15.5 per cent); occurring bilaterally in 10, more advanced on the right side in 5 and on the left side in 5, and unilaterally in 11, 4 on the right side and 7 on the left.

The variations and irregular ties in the contour of the articular surface of the sacroiliac joint, and the deviations in the plane of the joint surface at various levels of the joint in the same specimen and in different specimens, indicates that no one roentgenographic projection may be depended upon for its accurate visualization. For example, the upper part of the joint was visualized clearly on the roentgeno-

in the gross specimen, yet the articulation appeared intact roentgenographically.

#### CONCLUSIONS

The roentgenographic study of the lumbar spine and pelvis must be interpreted and evaluated with care. Limitation in the value of the oblique projection is suggested following comparative anatomical, pathological, and roentgenological studies on 25



Fig. 8. Early synostosis of the left sacrolliac joint; extra-articular ankylosis involves the capsule and anterior sacrolliac ligaments in the posterior-superior part of the articulation,  $\lambda$ , while the remaining portions of the joint are intact.

gram in only 6 out of 28 normal sacroiliac joints by means of the 45° oblique view. The results of diagnosis of partial and complete fusion in this articulation, even with careful stereoscopic views, is disconcerting. In the comparative anatomical and roent-genographic analysis of 25 lumbar spines and pelves previously mentioned, this diagnosis was correctly made on the roent-genogram in 6 specimens; in 4, synostosis was apparent on the roentgenogram but was not present in the gross specimen; while in 1, fusion of the joint was present

human lumbar spines and pelves, and is explained following anatomical and pathological observations of the articular facets and apophyseal (intervertebral) joints of the lumbar spine and the sacroiliac joints in 100 human cadavers.

#### REFERENCES

- 1. Ayres, C. E. Further case studies of lumbosacral pathology with consideration of involvement of intervertebral discs and articular facets. New England J. Med., 1935, 213, 716-721.
- 2. BAILEY, W. Anomalies and fractures of verte-

- bral articular processes. J. Am. M. Ass., 1937, 108, 266-270.
- 3. Beadle, O. A. The Intervertebral Discs. Medical Research Council, Special Report Series, No. 161. His Majesty's Stat. Off., London, 1931.
- 4. Вöнміс, R., and Ркévot, R. Vergleichende Untersuchungen zur Pathologie und Röntgenologie der Wirbelsäule. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1931, 43, 541-575.
- 5. Brooke, R. The sacrolliac joint. *J. Anat.*, 1923–1924, 58, 299.
- CALVÉ, J., and GALLAND, M. Intervertebral nucleus pulposus; its anatomy, its physiology, its pathology. J. Bone & Joint Surg., 1930, 12, 555-578.
- CHASIN, A. Die Dimensionen der destruktiven Veränderungen in den Wirbelkörpen, die Röntgenographisch bestimmt werden können. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1928, 37, 529-535.
- 8. Compere, E. L., and Keyes, D. C. Roentgenological studies of intervertebral disc; discussion of embryology, anatomy, physiology, clinical and experimental pathology. Am. J. Roentgenol. & Rad. Therapy, 1933, 29, 774-797.
- DITTMAR, O. Weitere Mitteilungen über Schragaufnahmen von Knochen und Gelenken. Röntgenpraxis, 1930, 2, 1022.
- Ferguson, A. B. Clinical and roentgenographic interpretation of lumbosacral anomalies. Radiology, 1934, 22, 548-558.
- 11. Fulton, W. S., and Kalbfleisch, W. K. Accessory articular processes of lumbar vertebrae. *Arch. Surg.*, 1934, 29, 42–48.
- 12. GHORMLEY, R. K. Low back pain, with special reference to articular facets, with presentation of an operative procedure. J. Am. M. Ass., 1933, 101, 1773-1777.
- 13. GHORMLEY, R. K., and KIRKLIN, B. R. Oblique view for demonstration of articular facets in lumbosacral backache and sciatic pain. Am. J. ROENTGENOL. & RAD. THERAPY, 1934, 31, 173-176.
  - 14. Grausman, R. I., and Sutro, C. J. Comparative radiologic and anatomic study of vertebral columns. *Am. J. Surg.*, 1935, 30, 551-554.
    15. Hadley, L. A. Subluxation of apophyseal ar-
  - Hadley, L. A. Subluxation of apophyseal articulations with bony impingement as cause of back pain. Am. J. Roentgenol. & Rad. Therapy, 1935, 33, 209-213.
  - Hadley, L. A. Apophyseal subluxation; disturbances in and about the intervertebral foramen causing back pain. J. Bone & Joint Surg., 1936, 18, 428-433.
  - 17. Hadley, L. A. Pathologic conditions of the spine; painful disturbances of intervertebral foramina. J. Am. M. Ass., 1938, 110, 275-278.
  - 18. Hibbs, R. A., and Swift, W. E. Developmental

- abnormalities at lumbosacral juncture causing pain and disability. Surg., Gynec. & Obst., 1929, 48, 604-612.
- 19. Hubbery, M. J. Oblique projection in examination of lumbar spine. *Radiology*, 1931, 16, 720—72.
- Johnson, R. W., Jr. Posterior luxations of lumbosacral joint. J. Bone & Joint Surg., 1934, 16, 867-876.
- 21. KAUFMANT, E. Pathologische Anatomie der malignen Neoplasmen. Deutsche Chir., 1902, 53, 384.
- 22. Kimberlet, A. G. Low back pain and sciatica; its etiology, diagnosis, and treatment. Surg., Gynec. & Obst., 1937, 65, 195-216.
- 23. Lachmarn, E. Roentgen diagnosis of destructive lesions of the knee joint and its limitations; experimental study. *Radiology*, 1938, 31, 521-5-6.
- 24. McMurmacz, J. P. The Development of the Human Body. P. Blakiston's Son & Co., Philadelphia, 1923, p. 169.
- 25. MEYER-BURGDOFF, H. Untersuchungen über das Wirbelgleisen. Georg Thieme, Leipzig, 1931.
- 26. MITCHELL, C. L. Isolated fractures of articular processes of lumbar vertebrae. J. Bone & Joint Storg., 1933, 15, 608-614.
- 27. Morton, S. A. Value of oblique view in radiographic examination of lumbar spine. *Radiology*, 193", 29, 568-573.
- 28. Nichols, B. H., and Shiflett, E. L. Uhunited anomalows epiphyses of inferior articular processes of humbar vertebrae. J. Bone & Joint Surg., 1933, 15, 591-600.
- 29. Oppenheimer, A. Narrowing of intervertebral foramina as cause of pseudorheumatic pain. *Ann. Surg.*, 1937, 106, 428-440.
- OPPENHEIMER, A. Diseases affecting intervertebral foramina. Radiology, 1937, 28, 582-592.
- 31. Oppenheimer, A. Diseases of apophyseal (intervertebral) articulations. J. Bone & Joint Surg., 1938, 20, 285-313.
- 32. Орреннеімея, A. Apophyseal intervertebral articulations, roentgenologically considered. *Radiology*, 19, 8, 30, 724-740.
- 33. Putti, V. New conceptions in pathogenesis of sciatic pain. Lancet, 1927, 2, 53-60.
- 34. Putti, V., and Logroscino, D. Anatomia dell' artritismo ver ebrale apofisario. Chir. d. org. di movimenzo, 1938, 23, 317-353.
- 35. Rendich, R. A., and Westing, S. W. Accessory articular process of lumbar vertebrae and its differentiation from fracture. Am. J. Roent-genol. & Rad Therapy, 1933, 29, 156–160.
- 36. Sashin, D. Critical analysis of anatomy and pathologic changes in sacro-iliac joints. J. Bone & Joint Searg., 1930, 12, 891–910.
- 37. Sashin, D. Interpertebral disk extensions into vertebral bodies and spinal canal. *Arch. Surg.*, 1931, 22, 527-5-7.

- 38. Schmorl, G. Ueber die an den Wirbelbandscheiben Vorkommenden Ausdehnungs- und Zerreissungsvorgänge und die dadurch an ihnen und der Wirbelspongiosa hervorgerufenen Veränderungen. Verhandl. d. deutsch. path. Gesellsch., 1927, 22, 250-262.
- 39. Schunke, G. B. Anatomy and development of sacroiliac joint in man. *Anat. Rec.*, 1938, 72, 313-331.
- SIMPSON, W. M. Diffuse vertebral metastasis of prostatic carcinoma without bony changes. Am. J. Roentgenol. & Rad. Therapy, 1926, 15, 534-541.
- 41. SMITH, A. DEF. Posterior displacement of fifth lumbar vertebra. J. Bone & Joint Surg., 1934, 16, 877-888.

- 42. Snure, H., and Maner, G. D. Roentgen-ray evidence of metastatic malignancy in bone. *Radiology*, 1937, 28, 172-177.
- 43. TESTUT, L. Traité d'anatomie humaine. 1. Octave Doin et fils, Paris, 1911.
- 44. Wagoner, G. Significance of horizontal transverse shadows of vertebral bodies as seen in lateral roentgenograms. Combined meeting of Orthopedic Section of New York Academy of Medicine and Philadelphia Orthopedic Club, Philadelphia, Nov. 18, 1938.
- 45. WILLIAMS, P. C. Reduced lumbosacral joint space. 7. Am. M. Ass., 1932, 99, 1677-1682.
- 46. WILLIAMS, P. C., and YGLESIAS, L. Lumbosacral facetectomy for post-fusion persistent sciatica. J. Bone & Joint Surg., 1933, 15, 579-590.



# DIAGNOSTIC PROBLEMS IN SURGERY OF THE UPPER URINARY TRACT\*

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IN THE urologic practice of today very few cases are not diagnosed correctly, making an exploratory operation a procedure of the past. We have means today not only to diagnose the anatomic phase of the upper urinary organs but also to visualize their physiologic mechanism in action, whether normal or abnormal. Intravenous urography has placed a most valuable method at the disposal of the profession at large and has freed the patient from the hesitancy and fear of an instrumental study.

Intravenous urography is gradually moving into the combined province of the practitioner of medicine and the roentgenologist. It is gratifying to note the alertness and care with which the technique and interpretations are carried out today. This special effort is undoubtedly due to the great responsibility felt by the roentgenologist in doing intravenous urography. He is conscious of the fact that success or failure depends upon proper diagnosis by urographic interpretation. The responsibility is felt even more when normality is to be diagnosed and pathology excluded. Often it takes more study and more care to prove a normal status of the urinary tract, than in complicated pathology.

We always ask for the repetition of this study whenever a doubtful point is at issue. It is much safer to do so than to dismiss it, since a single, often unimportant point, not completely answered, may be the main clue to the proper diagnosis.

We encounter many instances in which, after having exhausted the diagnostic means at our disposal, we are still confronted with the problems of the correct diagnosis. The classical symptomatology is not

always present. There may be a tumor without blood and a pyonephrosis without pus in the urine. A patient may have a renal colic without a stone and a stone without a colic.

# CYSTOSCOPY BEFORE UROGRAPHY IN HEMATURIA

While urography is the procedure of choice whenever a urological complaint is present, it is otherwise in hematuria. Here cystoscopy should precede urography in order to ascertain the exact source of bleeding. Most of the hematuric attacks are of short duration and often far apart. If the bleeding has stopped and unless there is frank pathology demonstrable, one is uncertain as to the correct diagnosis. We see such a condition quite frequently, especially in bleeding from the prostate gland. If the upper tract is found to be normal, it is assumed that the bleeding came from the prostate. This, however, may be erroneous and leaves one without a definite diagno-

There is no medical contraindication to cystoscopy during the bleeding stage. The still prevalent idea of waiting until the bleeding has stopped is fallacious and dangerous.

# ABDOMINAL AND RENAL PATHOLOGIES MASKING ONE ANOTHER

There are many instances of abdominal symptoms masking true renal disease, and vice versa, the renal symptomatology obscuring the true abdominal disease. We saw a patient with bilateral renal stones; a stone was removed from the left kidney while the suspected stone of the right kidney turned out to be a gallstone (Fig. 1).

<sup>\*</sup> From the Urological Service of the Mt. Sinai Hospital and the School of Medicine, University of Pennsylvania. Read before the Philadelphia Roentgen Ray Society, April 6, 1939.

There was another instance of renal stone in which, because of a few mottled spots on the pelvic bones, a malignant condition was suggested. Some vague abdominal pain was attributed to the renal calculus for which we treated the patient for

the existence of the gastric carcinoma was not suspected by the nephew of the patient, a very careful gastroenterologist. The few gastric symptoms of occasional nausea and eructation were attributed to the reflex irritation of the renal calculus.



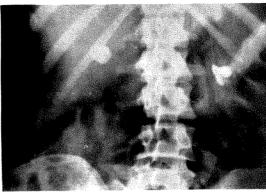


Fig. 1. Bilateral stones. The shadow on the left is renal calculus, the shadow on the right is gallstone.

years. Gastrointestinal study evealed an unsuspected carcinoma of the spenic flexure of the colon (Fig. 2).

We witnessed a similar occurrence in a patient already under anesthesia on the operating table for the removal of a renal calculus. The operation was postponed because of persistent vomiting during ether induction. The vomitus consisted of food ingested twenty-four hours earlier. Gastrointestinal study later revealed an extensive carcinoma of the stomach (Fig. 3). The symptoms in this case were so slight that





Fig. 2. Abdominal pain ascribed to a renal calculus was found to be due to carcinona of the splenic flexure of the colon.

In our study of ureteral calculi we found gastrointestinal symptoms in 29 per cent of the cases.

In a typical case of appendicitis being prepared for surgery, the easing of pain made the surgeon hesitant. A markedly ptosed kidney down in the iliac fossa with blockage due to kinking of the ureter was discovered later.

A young boy with backache and fever was treated for kidney disease over a period of several weeks. Complete study revealed congenital bilateral pelvic kidneys; the severe backache was found to be due to a tuberculous spondylitis of the eleventh and twelfth thoracic vertebrae (Fig. 4).

# DIFFERENTIAL DIAGNOSIS OF STONE IN THE URETER

The differential diagnosis of stone in the ureter and appendicitis is often very trying. It is a daily occurrence and taxes our ingenuity and sense of responsibility. I am certainly in favor of operating on the appendix whenever in doubt, but it is not such an innocuous procedure in the presence of stone. Although the presence of local tenderness is most significant, we have

seen it masked by the muscular spasm of a rapidly descending stone producing peritoneal irritation, because of the close proximity of the traumatized ureter to the peritoneum. Generally speaking, we believe that whenever the pain is severe a renal block should be suspected.

A patient entered the hospital with abdominal distention, generalized abdominal rigidity and no bowel movement for three days. A tentative diagnosis of intestinal obstruction was made and operation was thought to be imperative. Because of the poor general condition of the patient, the operation was postponed for several hours to give him medical care and Wangensteen drainage. He passed a stone and was promptly and completely relieved of all his symptoms. In a similar case we saw a colostomy done.

Carp, studying the symptomatology of 100 consecutive cases of ureteral calculus from our service, found a normal leukocyte count in only 10 per cent, while in 45 per cent of the cases the count was between 10,000 and 15,000. The evidence of leukocytosis in such a situation is therefore not absolutely indicative of appendicitis.

The classical urinary symptoms of frequency, dysuria, or hematuria may be expected because of the existing stone, and

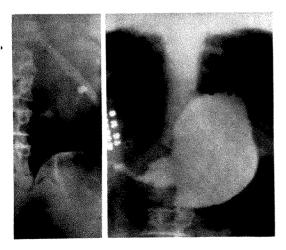


Fig. 3. Case of renal calculus on operating table. Operation deferred because of persistent vomiting during induction of ether anesthesia, Gastric carcinoma discovered later.

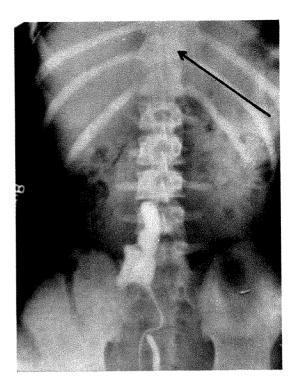


Fig. 4. Backache treated for renal disease. Both kidneys in polivis (congenital). Backache due to tuberculous spondylitis of eleventh and twelfth vertebrae (armow).

yet it is possable to be misled by their absence and stil have a stone lodged in the ureter. It can be said definitely that in most cases of stone in the upper and middle third of the ureter, bladder symptoms are absent or rare Definite bladder symptoms ensue when the stone has reached the lower third of the ureter.

Stones in the lower end of the ureter are frequently very small and faintly radio-paque and can be discerned only after proper preparation. Very frequently as in cases with a rapidly descending small renal calculus, a "pr mary calculus" (Randall), the shadow casting property is very low. We have learned not to expect a dense shadow, but to carefully scan the area for an irregular, faint y visible density. If in doubt, the passage of a catheter to the kidney will show waether obstruction with retention in the renal pelvis is actually present. We believe that the percentage of roentgen negative stones depends largely

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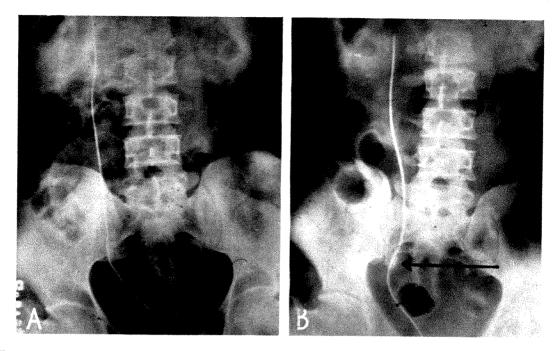


Fig. 5. A, stone in lower third of right ureter lying over the sacrum and invisible; B, stone visualized by exposure under varied angles, throwing the shadow downward.

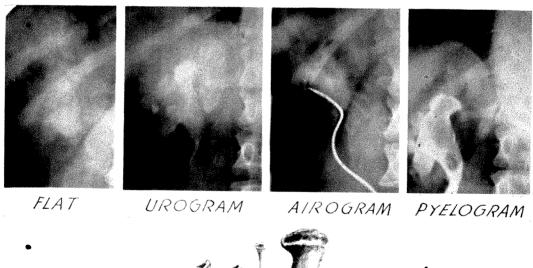




Fig. 6. Visualization of a faint shadow in the renal area by means of urography, pyelography and air injection. Large stone removed.

upon the care with which films are made and studied. In our series of ureteral stones, we found only 8 per cent non-opaque and 92 per cent casting a visible shadow.

Stones can be hidden by adjacent opaque structures, the ilium, the sacrum and the transverse processes of the vertebrae. These shadows should be carefully scanned for densities, as a stone overlying them can thus easily be overlooked. If there is a suspicion of such a density, the taking of seperal exposures under varied angles will throw the stone shadow away from the bone (Fig. 5).

Renal calculi, because of their age, are usually all radiopaque. Occasionally a case is found with a large renal stone casting a every faint shadow. Air injection into the



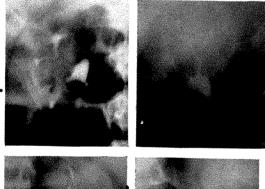




Fig. 7. "Irritable kidney." Spastic states of unknown origin in the normal urogram,

renal pelais will outline the faint calculus shadow (Fig. 6).

#### SPASTIC STATES

The regular rhythm of the nervous mechanism of the kidney may be disturbed producing alterations of the normal calyc-



Fig. 8. Spaam of the milking muscle of tae renal papillae.

eal and pelvic fillings. This is seen frequently bilaterally, but also unilaterally, one, two or al calyces imcompletely filled producing the effect of a thin spider web. We call it an 'irritable kidney,' assuming that the propelling mechanism works overtime, not permitting complete filling (Fig. 7).

Another phenomenon is observed when the spiral muscles of the calyces become spastic, cutting of a small amount of dye from the continuity of the pelvis. One or several calyces may thus be affected. It is a passing spasm and may not be found on a later studies (Fig. 8).

The pelvis proper may also be affected. We observed on the operating table a case of intermittent spastic contractions of the entire pelvis, appearing every fifteen to twenty seconds. The entire extrarenal pelvis would contract into a small hard ball ard disappear within the hilus of the kidney followed by complete relaxation. The

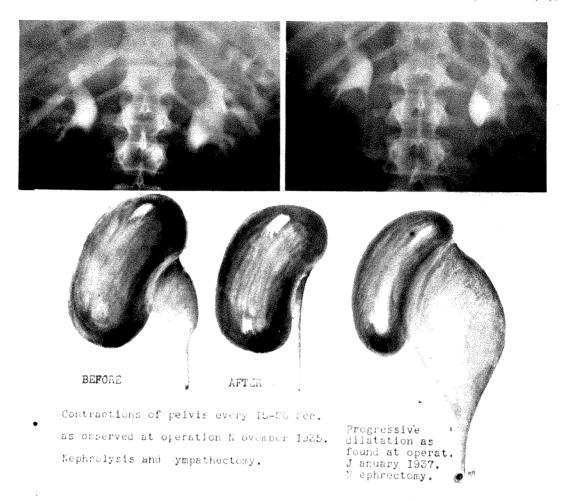


Fig. 9. Spastic contractions of the renal pelvis with varied density of pelvic filling.

Powerful contractions of pelvis observed on surgical exposure.

urograms in this case showed varied densities in pelvic filling (Fig. 9).

### EMERGENCY URCGRAPHY

There are instances of emergency when one must know definitely whether or not a given kidney is functioning, whether the high fever and severe toxemia are caused by the kidney in question or whether another focus is responsible for it.

This is especially true after operations upon bladder tumor. It and all has shown that in 50 per cent of cases of bladder tumor encroaching upon either ureteral orifice, there is a non-functioning kidney above.

This type of kidney cysfunction is rather

unusual. The kidney and pelvic architecture is unchanged or very slightly altered and yet no urine is being secreted. Randall coined the unofficial name of "NRA kidney" (no renal activity) denoting a "suspended animation." Function is restarted immediately after introduction of a catheter and is continued in definitely as long as adequate drainage is provided.

In many instances after removal of this catheter, following bladder tumor surgery, there remains a certain amount of edema of the ureteral orifice in the midst of coagulation necrosis with the resulting high fever, chills, and severe toxemia. Reinsertion of the catheter is imperative, but is frequently impossible cystoscopically owing to the

sloughing. Surgical drainage of the kidney is then the only choice. But the fever, chills, and toxemia may also be due primarily to the sloughing of the bladder wall with pericystitis and absorption, denoting inadequate bladder drainage and thus absolving the kidney entirely. We have resorted to intravenous urography in several such emergencies. The finding of a functioning kidney diverts our attention back to the bladder as the causative factor and avoids an unnecessary kidney operation.

# RENAL COLIC WITHOUT STONE OR STRICTURE

There are situations in which a typical renal colic is simulated by pathology other than stone or stricture. In the aged who have chronic obstructions at the bladder neck with weakened and dilated ureteral sphincters, there is observed a back pressure colic or "retrograde renal colic" (B. Lewis), which is instantly relieved after the bladder is emptied.

Renal coliz without stone is encountered

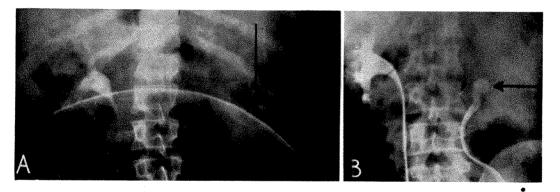


Fig. 10. A, huge "silent pyonephrosis"; B, ureteral stone w th "silent pyonephrosis."

Another emergency where intravenous urography proved of great aid was in a case of an elderly male with high fever and toxemia due to cystitis and bilateral epididymitis. He was complaining of pain in the right upper quadrant anteriorly. Examination showed the pain to be superficial and also on deep pressure. A renal block was suggested. Cystoscopy and catheterization of the right kidney was the only procedure of choice. We feared such a procedure because of the severe grade of infection of the bladder and adnexa, old age and severe toxemia. We resorted to an intravenous urography and were pleasantly surprised to find the kidney functioning well, without evidence of any obstruction. We therefore assumed the pain in the loin to be referred from a severe vasitis especially because of the superficial nature of the pain. The latter course proved this assumption to be correct.

at times in cases of true pelvic and ureteral hypermotility with rhythmic spasms, as previously stated.

Occasional y, severe pain in the loin is seen in fulminant epididymovasitis as described above.

Finally, the presence of a blood clot in the renal pelvis acting as a ball valve with typical renal colic must be considered. It is negative on the roentgenogram, but can be visualized as a filling defect by urography.

### STONES WITHOUT COLIC

Only smal stones freely movable will produce colic. If a stone is lodged within the ureter over a long period of time, the ureter having become dilated above and the passage of urine being free, no colic is noted. Slow and gradual destruction of the kidney will er sue with the development of a "silent pyonephrosis." Most of these cases present enough clinical evidence to be

easily diagnosed. There is, however, a recognized entity of "silent pyonephrosis" with practically no subjective symptoms, and because of complete blockage of the ureter no pus will be found in the urine. These cases of "silent pyonephrosis" are fever-free and show only a mild leukocytosis. We encountered several such cases in which a stone lodged in the mid-ureter, completely blocking the kidney, with a gradual accumulation of more than 1,000 cc. of thick, foul pus with complete absence

renal. The most common extrarenal cause is stone or postoperative constriction of the ureter. We encountered a postoperative fistula with a pyoureter caused by a huge stone within the ureter of long standing. Nephrectomy had been performed years before elsewhere. Vaginal ureterolithotomy brought about prompt closure of the renal fistula.

The cause of the fistula may lie in the kidney itself, as observed by us in one of our cases. We removed a fairly large stone

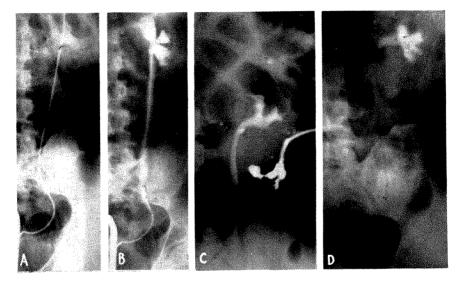


Fig. 11. Persistent renal fistula after nephrolithotomy due to complete occlusion of the calyceal communication with the main pelvis. Before operation: A, flat film with stone in lower calyx; B, pyelogram. After operation: C, pyelography and lipiodol injection into fistula, no filling of lower calyx; D, urography fills all calyces.

of symptoms (Fig. 10). We recall a characteristic case where a patient was treated for a suspected brain lesion, since there was no previous urinary history and the patient in a state of coma showed some cerebral manifestations. Because of a few pus cells in the routine examination of the urine and a previous experience by the physician in attendance, a urological investigation was suggested. A large "silent pyonephrosis" caused by an obstructing ureteral calculus was found and successfully drained, with ultimate recovery.

#### PERSISTENT RENAL FISTULAE

Renal fistulae after operations may be due to two main causes: extrarenal and

by nephrostomy from the dilated lower calyx, but the fistula refused to close. Careful study revealed no dye in the lower calyx on simultaneous retrograde pyelography and injection of the fistulous tract with lipiodol. Intravenous urography, however, revealed dye secretion within the silent calyx. We therefore assumed that the lower calyx became completely closed off from the main pelvis, acting as a pelvis for itself and draining its urine through the loin fistula. Breaking through the neck of the calyx into the pelvis promptly reëstablishing normal conditions (Fig. 11).

We encountered a third possibility of renal fistula. Following a nephrectomy, the details of which remained obscure, a loin.

fistula persisted for years. Intravenous dee appeared through the fistula and at operation we removed a small piece of renal tissue.

### PELVIC AND CORTICAL RENAL PAIN

Renal pain is characteristic and is caused by increased pressure within the pelvis due in whom pain persisted in spite of the finding of an empty kidney by catheter; at operation we found a subcapsular hemorrhage. We must also think of a sudden increase of pressure within a benign solitary renal cyst or within one of the many cysts in polycystic disease. Pain due to a cortical lesion of the kidney proper will be noted

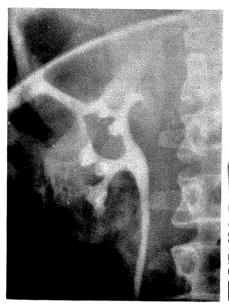




Fig. 12. Follow-up in a case of hematuria. Normal pyelogram (left), eight weeks later urography (right) reveals incomplete filling and extensive hypernephroma was found at operation.



to obstruction. The only sure way to prove that the pain in the loin is renal in origin is by the passage of a catheter into the renal pelvis. This procedure must remove the pressure and will cause instant relief.

In most cases the persistence of pain in the loin, in spite of an indwelling catheter, completely eliminates the kidney as the source of pain. There are, however, exceptions to the rule. We had two such patients only when the lesion has grown to such an extent as to put the renal capsule under tension.

### FOLLOW-UP UROGRAPHY

We believe in follow-up urography in all our surgical kidney cases and are either elated about the good results or dismayed about the failures. It enables the use of corrective surgery before it is too late.

Many pathological cases show improvement or regression very rapidly, others rather slowly. Thus we observed an unbelievably rapid infiltration of a kidney with hypernephroma within eight weeks (Fig. 12), and, on the other hand, we watched a case of staphylococcus sepsis by repeated urography gradually develop renal carbuncles after two months on one side and after two more months on the other side (Fig. 13).

was found occupying the entire abdomen, pushing the intestines to the upper corner of the opposite side. This hydronephrotic bag held more than 3,000 cc. of urine without causing any symptoms whatsoever.

#### COMMENT

We have attempted to show that we still have, and always will have diagnostic problems in surgery of the upper urinary tract. Refinement of technique and intelligent in-

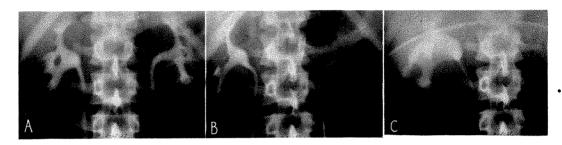
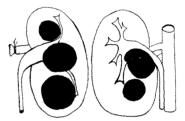


Fig. 13. Follow-up in a case of staphylococcus sepsis. A, normal; B, two months later, incomplete filling of the right kidney. Operation: Several larger carbuncles, nephrectomy. C, four months since normal urogram. Bulging of lower pole with displacement of ureter inward. Operation: huge liquefied carbuncles, drainage with complete recovery.

## GRAVE RENAL DISEASE WITH FEW SYMPTOMS

The symptoms in many cases of well advanced grave renal disease are few and often insignificant. We saw a child four years old with a congenital ureterocele of the bladder intermittently blocking both ureteral and urethral orifices, both kidneys having been completely reduced to thin shells with the capacity of a pint each, yet the only complaints were inability to gain weight and a slight pyuria. Although the phenolsulphonphthalein test was zero, there was enough renal tissue left to maintain life, as the blood urea nitrogen was still normal.

In another case, that of a man, aged seventy, with frequency of urination due to a benign enlargement of the prostate, while doing a cystogram an immense renal shell



terpretation of intravenous urography will lead to better surgical results in urology. But this is only possible when not only cooperation but also a special interest exists between the urological clinician and the roentgenologist in the search of a prompt, clear and complete solution of every problem presenting itself.

I want to thank Dr. Louis Edeiken for his intense interest, constant cooperation, and untiring efforts to bring out the many details which solved many of our difficult diagnostic problems.

#### CONCLUSIONS

- 1. Intravenous urography has placed renal diagnosis in the hands of the general practitioner and the roentgenologist.
- 2. Constant cooperation between the urologist and roentgenologist is necessary for detailed study of surgical cases.

- 3. In hematuria immediate localization of the source of bleeding by cystoscopy is imperative, to be followed by urograpay later.
- 4. A thorough examination should precede every surgical kidney case to eliminate coexisting abdominal disease.
- 5. The high percentage of leukocytos s in ureteral calculus is stressed, especially when diagnosing appendicitis.
- 6. The poor shadow casting properties of small ureteral calculi and their position behind bony structures is discussed.

- 7. Rena colic without stone and stone without colic are encountered.
- 8. "Siler t pyonephrosis" is not infrequently seen and is remarkably asymptomatic.
- 9. Emergency urography is of great value in differential diagnosis of obscure toxemia and fever.
- 10. Spastic states of the renal musculature are discussed.
- 11. Rapic and slow progression of renal pathology is demonstrated by follow-up urography.



## GASTRODUODENO-COLIC FISTULA: CARCINOMA OF TRANSVERSE COLON

By MAXIMILIAN J. HUBENY, M.D., F.A.C.R., F.A.C.P.

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ASTROCOLIC fistula was first discovered by Murchison. 13 The majority of such fistulas are caused by malignant lesions in the greater curvature of the stomach; the next most frequent cause is a jejunal ulcer developing at the site of a gastroenterostomy stoma. Goløb4 found almost half due to the latter cause. In 21 cases reviewed at the Mayo Clinic 19 occurred after gastroenterostomy and 2 from carcinoma of the colon. Kohlmann<sup>7</sup> adds to the etiologic factors carcinoma of the splenic flexure of the colon, perforation of a duodenal ulcer, tuberculous peritonitis and suppurative cholecystitis. Rees12 mentions typhoidal ulcer of the colon. Langemeyer<sup>8</sup> describes a case in which gastrojejuno-colic fistula developed after gastroenterostomy and, in trying to work out the pathogenesis, confesses that some of it "bleibt unklar." Peptic ulcers, wherever situated, seem to have this tendency to form sealed communications with adjacent viscera, Moiroud9 even recounting a case in which the iejunum became fixed to the lesser curvature of the stomach at an ulcer site, taking on thereby some of the characters of a surgical stoma, and markedly ameliorating the patient's symptoms!

Perforation, as described by Morley, Brooke and Little, <sup>10</sup> would seem relatively uncommon.

The diagnosis of gastrocolic fistula, or duodenocolic fistula, or a combination of the two, is more often arrived at roentgenologically than by clinical methods, though there are some fairly constant clinical manifestations.

Diarrhea is the most common and Streicher<sup>13</sup> urges a search for such a fistula in all cases presenting obscure diarrhea. The diarrhea is lienteric in type. One case of

night blindness<sup>14</sup>—a deficiency disease and in this case developing in a patient receiving an adequate diet)—was finally found to be due to the food loss resultant upon a gastrocolic fistula. The night blindness disappeared after surgical removal of the fistula. Breitner<sup>1</sup> recorded a case in which the patient developed paresthesias.

When the condition follows gastroenterostomy, eight to nine years has been the average time, though it was only six months in a case described by Polya.<sup>11</sup>

So far as the roentgenologic approach is concerned, the condition shows up much better and much more frequently with a barium enema than following a meal, in the experience of most observers. <sup>4,13</sup> One reason advanced for this is the probable formation of a mucous membrane fold <sup>13</sup> which has a ball-valve action and interferes with the egress of the barium from the stomach.

Very great confusion may arise in the giving of a meal, moreover, as in the case described by Rees,12 where the passage of barium into the gallbladder from a gastroduodeno-colic fistula was taken merely to be an incompetent sphincter of Oddi. In another case described by Feldman,<sup>3</sup> an enema was altogether misleading, since a fistula from the colon to a kidney was productive only of a filling defect which seemed quite typical of carcinoma (particularly since the patient had a mass in that area). The enema failed of aid in the case of Morlev, Brooke and Little<sup>10</sup> because it could not be sent farther than the descending colon. Early, Holzknecht<sup>6</sup> suggested introducing air into the rectum in the hope that ' it would fill out the "Magenblase."

In the 21 cases described at the Mayo Clinic,<sup>4</sup> the roentgen ray gave positive evidence in 11, doubtful evidence in 1, and was

relatively negative in 8. Diagnosis was made clinically in 9.

#### REPORT OF CASE

A. J., female, housewife, aged forty-five, of Lithuanian decent. For four and a half months she had complained of weakness, loss of weight, and intractable diarrhea. Food that she ate was passed sometimes in only a few minutes. Her past history, so far as surgery was concerned, was negative.

She entered Cook County Hospital on December 19, 1938, and was sent to the roentgen department on December 27 for barium enema.

As the colon filled, we thought we noticed an irregularity in the transverse colon, close to the hepatic flexure. Its outline was indistinct, and we reserved judgment until we could see the films.

The films showed the stomach distinctly outlined. Though we considered a ball-valve action as one of the possibilities in this delay (for we had seen no stomach outline in the roentgenoscopic room) we were also obliged to consider the possibility of there being a union between the pars descendens of the duodenum

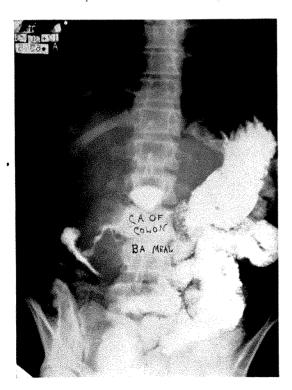


Fig. 1. Roentgenogram after administration of an opaque meal.

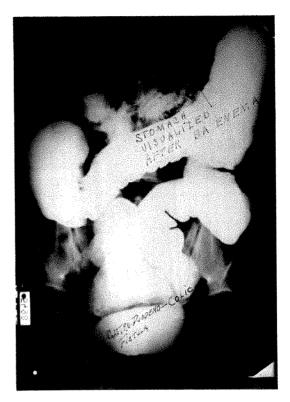


Fig. 2. Stomash visualized after barium enema.

and the colon, with no direct connection between stomach and colon.

We sent for the patient as soon as the previous barium could be well cleaned out, and this time gave a barium meal. The nature of the communication was by no means distinct as we watched the progress of the meal. The first portion of colon to show an outline was in the region of the splexic flexure. (The lesion, we already knew, was near the hepatic flexure!) We were at length able to demonstrate that the barium was entering near the hepatic flexure and being swiftly carried along to the splenic flexure. An outline of small bowel next became distinct, but only after tedious observation. We could demonstrate no direct connection between stomach and colon. Films showed stomach, small bowel and colon and did not serve greatly to clarify the condition.

The patient went to operation soon thereafter, and the entire region of the hepatic flexure was found encared in a large mass, with camentum drawn anto it, and all minute anatomical relations atterly obscured. The mass was dissected free, and the necessary repair nade in stomach, tolon and small bowel which

were implicated. The patient did very poorly after the operation and died on January 7, 1939.

The preliminary report of the surgical pathologist was to the effect that the relationship of the fistula in the specimen was impossible to describe until there was m croscopic evidence for the structures involved, since it was so bound in inflammatory tissue.

The pathologist's report follows: "The specimen consists of a portion of small intestine 18 cm. in length by 3.5 cm. in circumference. The serosa is pale-gray to dark-red. The wall is edematous. The mucosa is pink-red to red in color. In addition there is a portion of transverse colon to which is attached the great omentum. At one pole the large bowel is transformed into a raised cauliflower mass 10×9 cm. in dimension. The edges of this mass are raised above the mucosa 2 cm. and are light gray to red in color. The mid portion of this mass forms a defect of 4 cm. which continues with the lumen of what appears to be the stomach near the duodenum. The mucosa here is likewise thrown up into a papillomatous mass similar to that described in the large intestine. Microscopic section of the colon reveals a mucus-producing infiltrating adenocarcinoma extending into the duodenum and stomach thus forming a \_astroduodeno-colic fistula."

#### SUMMARY

- 1. A gastroduodeno-co ic fistula is described, which presented some difficulty in the roentgen diagnosis.
- 2. The lesion developed from a primary carcinoma of the transverse colon.
- 3. The principal symptom, in common with most of the cases described by others,

was sudden diarrhea after the taking of any food.

4. The perifocal inflammatory reaction obscured the anatomic relations at operation and it was necessary to mobilize the mass as such.

#### REFERENCES

- Breitner, B. Zur Symptomatologie der gastrokolischen Fistel. Schweiz. med. Wchnschr., 1938, 68, 443-444.
- 2. Burnham, M. P. Roentgen disgnosis of gastrocolic and duodenocolic fistulae. Am. J. Roentgenol., 1917, 4, 173-179.
- 3. FELDMAN, M. Renocolic fistula. Am. J. Digest. Dis. & Nutrition, 1937, 4, 110-112.
- 4. Golob, M. Gastrocolic fistula. *Am. J. Surg.*, 1930, δ, 1007–1009.
- 5. Groeschel, L. B. Gastrocolic fistula. Am. J. Roentgenol., 1921, 8, 516-520.
- 6. HOLZKNECHT. Quoted by Burnham, ref. 2.
- 7. Kohlmann, G. Die Klinik und Röntgendiagnose der Duodenal-Kolon-Fistel. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1925, 33, 554-561.
- 8. LANGEMEYER, C. Ueber einen Fall von ungewöhnlicher Magen-Kolonfistel. Zentralbl. f. Chir., 1938, 65, 1168-1172.
- MOIROUD, P. Les fistules gastro-duodénales spontanées au cours de l'évolution de l'ulcère de la petite courbure. Presse méd., 1935, 43, 1249-1251.
- 10. Morley, H. S., Brooke, R., and Little, C. J. H. Gastro-jejuno-colic fistula with terminal perforation into the peritoneal cavity. *Lancet*, 1936, 1, 1065–1066.
- 11. Polya. Quoted by Breitner, ref. 1.
- 12. REES, C. E. Duodenocolic fistula with incompetent sphincter of Oddi. J. Am. M. Ass., 1933, 100, 496-497.
- 13. Streicher, M. H. Diarrhea—gastro-colic fistula. *Illinois M. J.*, 1938, 73, 77-78.
- 14. WILBUR, D. L., and EUSTERMAN, G. B. Nutritional night blindness. J. Am. M. Ass., 1934, 102, 364-366.



# MICROTIA AND CONGENITAL ATRESIA OF THE EXTERNAL AUDITORY CANAL

# DEMONSTRATION OF THE EXTERNAL AUDITORY CANAL BY MEANS OF TOMOGRAPHY

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ROUTINE roentgenograms of the temporal bone do not reveal the external auditory canal clearly or consistently. Occa sionally, it may be visualized in the Towne projection by using a higher kilovoltage but, at best, the outlines of the canal are indistinct because of the superimposition of the shadows of other structures. If the bone is undeveloped or sclerotic, it may be impossible to show the canal at all.

Our results in a recent study of the temporal bone by means of a simple tomograph of the type described by the late E. W. Twining¹ suggested that the method might be of value in the demonstration of the external auditory canals. Our interest was further stimulated by four recent patients who were suffering from microtia. In all four cases, the tomograms clearly revealed a complete atresia of the external auditory canal accompanying the deformity of the pinna.

The technique used is primarily designed to show the external auditory canal in two planes. Because the long axis of the canal lies in the coronal plane, a tomogram made at the appropriate level in this plane will show the canal in its entire length (CS, Fig. 1). A second section through a plane at right angles to this will show the canal in cross section  $(SS_3, Fig. 1)$ .

### TECHNIQUE

1. Coronal Section (CS, Fig. 1). The patient lies on the back with the occiput

<sup>1</sup> Twining, E. W. Tomography, by means of a simple attachment to the Potter-Bucky couch. *Brit. J. Radiol.*, 1937, 10, 332-347.

against the table and the sagittal suture in the midline. The orbitomeatal line should be perpendicular to the plane of the table top. The apparatus is then adjusted so that

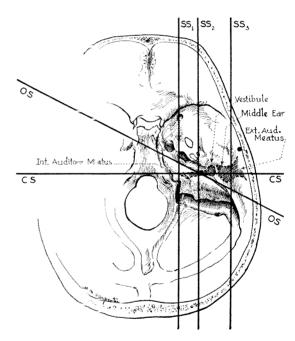


Fig. 1. Norma basalis of skull (diagrammatic) illustrating the planes of section through the temporal bone and their relation to the internal anatomy of the bone. The levels \$\$S\_3\$—sagittal section, and \$\$C\_2\$—zoronal section, are used for this study.

the plane of the section will pass through the external auditory canals, the height of which above the table top is measured directly on a scale with the patient in position. It is essential to have the head straight, because any rotation will throw

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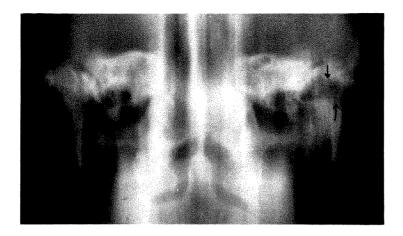


Fig. 2. Coronal plane section, revealing complete atresia of the external canal on the right side (arrows indicate the normal canal on the left). In the negative the right and left sides are reversed.

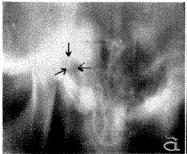
the opposite canal out of the plane of the section, and it will not be revealed for comparison. We have found an exposure of two seconds at 50 ma. using the Potter-Bucky diaphragm very satisfactory.

2. Sagittal Section. The patient lies prone the head being rotated until the sagittal plane is parallel with the table top, the affected ear down (this is the position for routine lateral roentgenograms). The tomograph is then adjusted to select a plane 2.5 cm. above the level of the table top (883, Fig. 1). This, in the ordinary sized head, will give an image of the canal in cross section, 0.5 to 1.0 cm. lateral to the tympanum. If indicated, further films may be made at other levels. For comparison, films of the opposite side at the same levels should always be made.

#### COMMENT

The films obtained with this technique have all been of diagnostic quality. The coronal section film (Fig. 2) reveals the ex-

ternal auditory canal on the normal side in its long axis, and demonstrates the absence of a canal on the affected side. Any attempt to interpret tomograms of this region without a normal for comparison is unwise. In some films in this plane, the middle ear and the internal canal are also seen. The sagittal section ( $SS_3$ , Fig. 1) shows the normal canal in cross section (Fig. 3a), together with the temporomandibular joint and the mastoid process. The absence of a corresponding external canal shadow on the affected side (Fig. 3b) is obvious. In the interpretation of films made in this projection, there is one source of confusion. If the section has been made through the depths of the canal, close to the tympanum, the middle ear, though strictly not in the plane of focus, may be revealed as an indistinct rounded shadow (Fig. 3b) which may be • confounded with the external canal proper, when the canal is in fact absent. On comparison with the normal side, however, it will be noted that a normal canal is irregu-



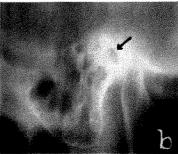


Fig. 3. Sagittal plane sections 2.5 cm. above table top: *a*, with unaffected side (left) down, revealing a normal external auditory canal in cross section (indicated by arrows); *b*, with affected side (right) down, revealing no evidence of external auditory canal. Arrow indicates shadow of tympanum.

larly ovoid in cross section rather than round, and that its boundaries are clearly defined, not blurred. If there is any doubt, a further section made more lateral will eliminate the hazy shadow of the middle ear.

There seems no good embryologic reason why microtia should not occur as an solated defect, but the fact remains that in the majority of cases there are associated lesions, either the common atresia of the external canal or some defect in the auditory ossicles or even the labyrinth. Treatment of these patients is therefore limited as a rule to plastic operations on the deformed pinna, and it is generally agreed that surgical interference with the bone is useless owing to the frequency of concomitant defects. It is, however, possible that

there are cases in which the external canal is present and in which hearing is reasonably good, and in these some form of repair might be considered. In such cases, a tomogram would be of the utmost value in giving the surgeon knowledge of the state of development of the canal. From the point of the roentgenologist, too, it is satisfying to be able to offer an anatomic diagnosis. We might remark parenthetically that we have not been able to demonstrate the ossicles by tomography, nor, on general grounds, does it appear to be feasible, at least with the simple apparatus used in this study.

No dould the method would also be useful in the investigation of atresia due to trauma, infection, and so on, and in the demonstracion of osteomas of the canal.



# ROENTGENOLOGICAL AND PATHOLOGICAL CONSIDERATIONS OF EWING'S TUMOR OF BONE\*

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ONSIDERABLE confusion exists re-✓ garding the clinical, roertgenological and histological criteria for the exact diagnosis of Ewing's tumor of bone. In 1922, Ewing<sup>1</sup> designated as a distinct type among primary bone neoplasms, a tumor arising, in his belief, from the perivascular lymphatic endothelium occurring, as a rule, in voung individuals and known to be radiosensitive. Although this neoplasm is still referred to as Ewing's endothe ioma of bone by some authors, many pathologists have doubted its endothelial origir. Several examples of primary bone tumor have been selected from the case record file of the University Hospital illustrating the difficulties which may be encountered in the differential diagnosis of this tumor. No attempt has been made to gather all tumors of this type from the available records. Individual cases have been selected either as typical Ewing's tumors presenting the cardinal features of this lesion or as tumors of some other type in which differentiation has been difficult.

Roentgenograms in a classical example of Ewing's tumor show the lesion located usually in the diaphysis or metaphysis of long bones. The patient is usually less than twenty-five years old, and pain, swelling, low grade fever and leukocytosis are common clinical findings. Roentzen findings in early tumor development show slight thickening and increased density of bone cortex. Later, mottled rarefaction and periosteal reaction showing lam nation parallel to the long axis of bone ma occur. In still later stages there may be swelling of soft parts, more bone destruction and rarely infiltration of the epiphysis. The only alteration found in the marrow cavity is irregularity and narrowing due to thickened cortex. Pathological fracture rarely occurs. The tumor is extremely raciosensitive.

Atypical variations of Ewing's tumor are often encountered. In these, roentgen examination may show only bone lysis or sclerosis. Unusual sites of origin such as spine, clavicle, skull or pelvis may be encountered. When the tumor arises in flat bones, lysis is commonly the only roentgen evidence of disease. Periosteal reaction may be absent or when present may take the form of spicule formation perpendicular to the shaft, a common sign in osteogenic sarcoma.

Necessary roentgenological differential considerations where Ewing's tumor is suspected must include any disease process which may produce any of these bone changes. There are several such lesions which must be considered. Chronic osteomyelitis and syphilitic osteitis must be ruled out and metastatic neoplasm may be confusing, particularly when found in long bones. Since tuberculosis involves the epiphyses primarily, differentiation is usually not difficult though close similarity may exist in the case of tarsal or carpal lesions. Bone involvement in leukemia is rarely solitary. In Hodgkin's disease the epiphysis is commonly involved and pathological fracture is prone to occur. Metastatic neuroblastoma and xanthomatosis must be considered, particularly in children. It is readily seen, then, that while roentgen changes may strongly suggest Ewing's tumor, confirmatory clinical and pathologic data are necessary before a definite diagnosis can be made.

The typical microscopic appearance is said to be the only constant finding in Ewing's tumor. Though this is true in some degree, the histopathology may be as variable and confusing as the roentgenogram. In the classical example, sections show dark staining round cells closely packed with practically no intercellular reticulum. The cell has

<sup>\*</sup> From the Department of Roentgeno bgy, University Hospital, Ann Arbor, Michigan.

a very thin rim of cytoplasm, a large nucleus with thin nuclear membrane and chromatin arranged in no particular pattern. In bone, masses of tumor cells invade lacunar spaces where osteoid tissue and osteoblastic activity give evidence of reactive bone formation. Osteoclasts may be found about the margins of dead bone. The tumor cells in this neoplasm do not form bone.

In atypical tumors cellular monotony is less marked and varying amounts of intercellular substance may be observed. Occasionally tumor cells show cytoplasmic processes and hyperplastic reticulo-endothelium may be present.

For an experienced pathologist differentiation between malignant neoplasm and inflammatory reaction is not difficult, and correct interpretation of the classical histologic characteristics of Ewing's tumor is easily made. However, in those tumors where histological findings are atypical, exact classification is often impossible. In many instances, without the aid of clinical knowledge it is impossible to definitely classify the neoplasm as belonging to the Ewing tumor group since the histology differs in no way from that of round cell sarcoma arising in other tissues.

Biopsy should never be omitted when Ewing's tumor is suspected. Reports to the contrary notwithstanding, there is no clinical or experimental evidence that this procedure causes dissemination of tumor cells. Incisional biopsy should be done if possible, the aspiration method being used only as a last resort.

Five tumors have been selected for presentation which are sufficiently characteristic to be considered true Ewing's tumors. The first occurred in a boy, aged fourteen, involving the proximal metaphysis of the left tibia. Roentgenograms showed both increased density and rarefaction in the cortex. Elevation of the periosteum with parallel and perpendicular bone production was present. Though infiltration extended almost to the epiphyseal line there was no invasion of the epiphysis. Since pulmonary metastasis was demonstrable at first examination, amputation was not advised and ir-

radiation was administered to the neoplasm with good local response. This patient is alive six months after the onset of symptoms.

The next two neoplasms were located in the fibula. The first of these developed in the diaphysis of the left fibula of a boy, aged thirteen. Roentgenograms showed cortical thækening and increased density with some distortion of the marrow cavity. There was irregular periosteal reaction without lamination, and extensive infiltration of soft rissues (Fig. 3). Death occurred four month, after amoutation. The other Ewing's tun or arising in the fibula showed mottled increased bone density but the predominant almormality was lysis. Parallel deposits of subperiosteal bone as well as perpendicula-spicules were present. Neither epiphysis was involved. The localized bone destruction suggested subperiosteal origin.

The next lesion (Fig. 1), although typical enough from the histopathological viewpoint, presented a very unusual roentgenological appearance. The tumor seemed to have arisen in the second cuneiform as shown by complete lysis of this bone with less extensive destruction of neighboring bones. Soft tissue swelling of the entire foot was obvious. A diagnosis of tarsal tuberculosis was made at the time of the first roentgen examination, the true identity being learned by aspiration biopsy. Following biopsy and amputation of the foot, the tumor recurred in the upper tibia and fibula and metastases were found in the lungs. Eleven months after onset of symptoms this patient died

The next Ewir g's tumor was one arising in the distal half of the clavicle. Clinically and roentgenologically this lesion was first diagnosed acute osteomyelitis. Bone rarefaction was the predominant abnormality seen in the roentgenogram though there was some cortical thickening and thin subperiosteal bone deposit. Following biopsy of the clavicle, fractionated irradiation was given with relief of pain and some roentgenological evidence of favorable response. Death occurred ten months after

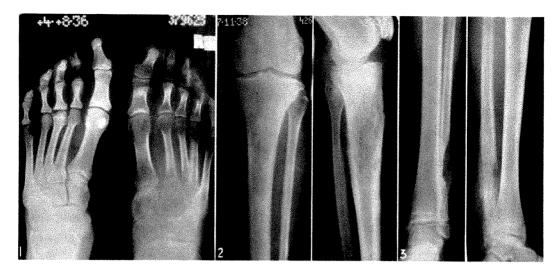


Fig. 1. (379623) Ewing's tumor apparently arising in second cuneiform infiltrating surrounding soft tissue and bone.

Fig. 2. (426629) Primary malignant bone neoplasm arising in metaphysis of tibia in a male aged sixty-four in which the histology is compatible with Ewing's tumor.

Fig. 3. (412923) Ewing's tumor arising in lower fibula showing bone lysis and periosteal reaction. Appearance suggests periosteal origin.

onset of symptoms, with clinical evidence of generalized metastases.

The histopathology was so similar in these five tumors that material from one case will serve for demonstration. With low power magnification (Fig. 6) this tissue is seen to be made up of small dark cells quite closely packed with no intervening intercellular substance. More highly magnified (Fig. 7), the cells are found to be round with large dark-staining nuclei and no nucleoli. A section through bone (Fig. 8) shows invading tumer cells occupying the lacunar space, a portion of which contains osteoid tissue. Active osteoblasts are seen about the margins of the bone but there is no evidence of tumor bone formation. Other fields show islands of dead bone surrounded by osteoclasts. Reactive bone formation in response to invading tumor tissue explains the zones of increased density seen in roentgenograms. Osteoclastic absorption of dead bone accounts for the appearance of patchy bone lysis.

The next two examp es represent lymphoblastoma involving bone. The first of these involving the upper portion of the left humerus occurred n a male, aged sixtyfour, showing generalized lymphadenopa-

thy. Roentgen examination disclosed a motheaten appearance of the entire upper third of the humeral shaft and pathological fracture. Mottled increased density and cortical irregularity extended into the epiphysis. There was no evidence of periosteal reaction. A roentgenogram eighteen months after irradiation showed healing of the fracture, decreased sclerosis and widening of the marrow cavity. Continued disability due to soft tissue edema prompted amputation one year later. The patient is still living six years after onset.

The other lymphoblastoma of bone (Fig. 4) occurred in a male, aged forty-five, whose first roentgenograms showed motheaten destruction in the coracoid process and neck of the scapula and also in the neighboring humeral epiphysis. There was also destruction and compression of the tenth dorsal vertebral body. Both shoulder and spine areas were irradiated with satisfactory symptomatic relief. A few months later bilateral axillary and supraclavicular lymphadenopathy developed.

Roentgen changes in both of these cases resemble those found in Ewing's tumor; however, the age of these patients, the demonstration of epiphyseal involvement and the occurrence of pathological fracture are more characteristic of Hodgkin's disease.

Sections from the first of these, while somewhat atypical, showed a histopathologic picture compatible with Hodgkin's disease. Cells varied widely in size and shape, had abundant cytoplasm and were embedded in a rather dense bed of hyperplastic reticulo-endothelium. Sections of the soft

atypical lymphoblastoma a more likely diagnosis. Undifferentiated lymphoblastoma is very similar to atypical Ewing's tumor in histopathological appearance.

The next two examples of primary bone neoplasm are shown because accurate histological classification is impossible. In the first, a boy aged nine, the body of the sixth dorsal vertebra was involved and surrounded by soft tissue infiltration. Roent-



Fig. 4. (372821) Mottled rarefaction and increased density occurring in the coracoid process of the scapula and head of humerus due to lymphoblastoma. Similar changes in tenth dorsal body with compression deformity.

tissues of the arm made following amputation showed extensive Hodgkin's infiltration throughout the material examined. The bone showed no evidence of tumor invasion. All of the lacunar spaces were filled with fibrous connective tissue. It is conceivable that irradiation may have completely destroyed invading tumor cells in bone—there is no reliable histopathological evidence for or against this contention.

In the second example of lymphoblastoma of bone, biopsy material was obtained from the scapula and the histopathologic classification was much more difficult. The sections showed infiltration of soft tissues and bone by a neoplasm made up of cells of various sizes and shapes with some intercellular substance. In several areas of this section the histologic appearance was compatible with that of Ewing's tumor. However, variability in cell shape and size plus the presence of reticulo-endothelium made

genograms shawed compression deformity with narrowing of the anterior and left lateral margins of the body. There was also marked narrowing of the intervertebral space, particularly on the left. The principal bone change here was one of increased density though some rarefaction was seen in the ribs adjoining the involved vertebra.

The other tamor also occurred in the spine of a boy aged nine (Fig. 5). Roent-genograms showed increased density of the first lumbar body, obliteration of the intervertebral space chiefly on the right, together with kyphos deformity. There was also posterior displacement of the first lumbar body as viewed in lateral projection. Increased censity and destruction of a vertebra is a very uncommon finding in a patient of this age, scarcely compatible with tuberculoss or xanthomatosis. The original roentgenological impression was metastatic neoplasm. Death occurred two

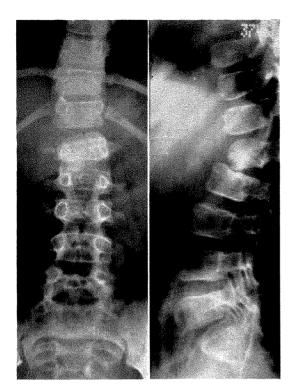


Fig. 5. (374668) Lysis and increased density in first lumbar body with narrowing of intervertebral space, and some posterior displacement caused by a tumor, the histology of which is compatible with Ewing's tumor.

years after onset of symptoms with clinical evidence of pulmonary metastasis.

In both of these tumors material for microscopic study was obtained from the tumor infiltrated soft tissues over the spine (Fig. 9). Sections show small, round, darkstaining cells infiltrating all of the tissue removed. They are quite widely spaced and show abundant intercellular substance, a portion of which is collagen from the infiltrated soft tissue. Some of the cells show cytoplasmic processes. The histopathology in both tumors, while quite atypical, is compatible with Ewing's tumor.

As pointed out by Colville and Willis' and Rix and Geschickter,<sup>3</sup> there is marked similarity in the microscopic appearance of Ewing's tumor and sympathoblastoma. The latter authors have recently reviewed all of their previously reported Ewing's tumor cases involving the spine and have found them to be sympathoblastomata. The tissues in the two tumors just de-

scribed were stained with Masson's trichrome stains and Roger's silver impregnation method but failed to demonstrate any evidence of cell type compatible with sympathogonia in any of the various stages of differentiation. With the information available, these two tumors must be classified as round cell sarcomata, the general appearance of which is compatible with atypical Ewing's tumor.

There is marked variance of opinion regarding the histogenesis of Ewing's tumor. Ewing¹ originally believed the tumor rose from the perivascular lymphatic endothelium. Connor⁴ points to the reticulo-endothelium as the tissue of origin. Geschickter and Copeland⁵ state that the tumor is lymphocytic in origin, and Roome and Delaney⁶ consider the neoplasm related to myelocytoma. There is also marked difference of opinion regarding the portion of bone in which the tumor arises. Some believe origin is within the cortex, others in the periosteum and still others believe it is within the bone marrow.

Study of the present material indicates that the tumor arises in the cortex or beneath the periosteum. In two of the neoplasms, even though they were advanced, roentgenograms showed the marrow cavity, though irregular, to be visualized throughout the entire length of the shaft. One would expect that a tumor arising in the bone marrow would produce enlargement of the cavity and thinning of the cortex, a condition which is not encountered in Ewing's tumor.

In bone sarcomas which are clinically and roentgenologically typical Ewing's tumor, the histopathology may differ widely from that usually considered characteristic. An unusual pathological picture, for example, was seen in a tumor arising in the proximal metaphysis of the tibia in a male aged sixty-four (Fig. 2). The roentgenograms showed motheaten lysis and some increased density in the upper tibia. There was a very slight degree of periosteal thickening and no evidence of subperiosteal bone production. The sections showed undifferentiated cells bearing many of the morpho-

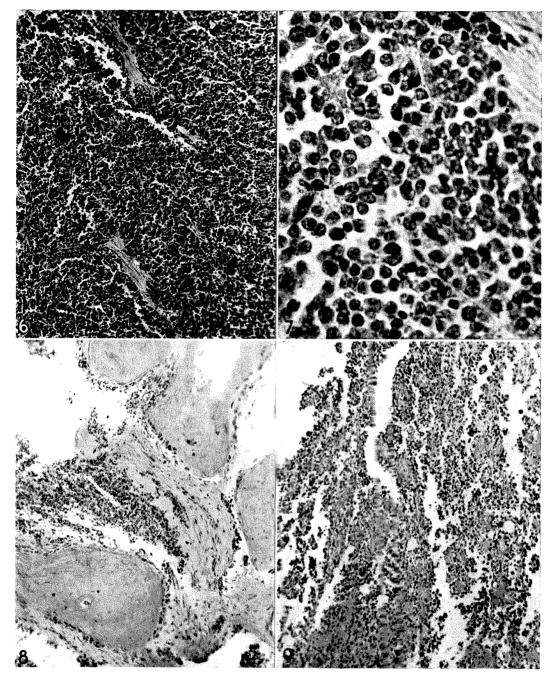


Fig. 6. (422806) Low power photomicrograph showing classical appearance of Ewing's tumor made up of small dark staining round cells with little intercellular substance.

Fig. 7. (422806) High power photomicrograph of same tumor.

Fig. 8. (422806) Appearance of same tumor in invaded bone. Lacunar space contains both tumor and oste-oid tissue.

Fig. 9. (374668) Low power photomicrograph of neoplasm arising in first Limbar body. Section was taken from infiltrated soft tissue adjacent to spine.

logical characteristics of Ewing's tumor. They were uniform in size and shape but loosely arranged, many showing a tendency

to spindle shape and there was abundant ir tercellular reticulam. The appearance of these areas was typically that of undiffer-

entiated fibrosarcoma. There were no tumor giant cells and no tumor bone formation.

There are undoubtedly some who would object to classing this neoplasm as a Ewing's tumor because of age of the patient and atypical histopathology. However, the roentgen findings are compat ble with Ewing's tumor and in certain areas the histopathology is fairly typical. A tumor slightly more differentiated might conceivably form bone and would then be classed as an osteogenic sarcoma.

All of this supports the contention of Melnick<sup>7</sup> who maintains the cell of origin in Ewing's tumor is the undifferentiated mesenchymal cell which, ir postnatal life is found about small blood vessels and capillaries. In accordance with this conception, classical Ewing's tumor is an undifferentiated round cell sarcoma composed of cells not yet differentiated sufficiently to form reticulum. In atypical neopiasms where tumor cells may be slightly nore differentiated, they may assume norphologic and physiological properties of the fibroblast or fibrocyte, become spindle shaped, produce reticulum, and, with still more cellular differentiation, possibly form bone. On the other hand, differentiation may proceed along another line with production of reticulo-endothelium and myelocytic elements and may resemble the histologic picture found in lymphoblas toma. The cell of origin, then, in Ewing's tumor, fibrosarcoma, osteogenic sarcoma and lymphoblastoma is the same, histopathological classification depending on the line and extent of differentiation of tumor cells. The division of the clinical entities becomes arbitrary and must be based on cinical, roentgenological and histopatholog cal criteria.

If, as is suggested, Ewing's tumor is an extremely undifferentiated round cell sarcoma of bone the question arises—is such a separate classification justified? It would seem that this clinical grouping is justifiable and serviceable provided it is under-

stood that this designation does not imply a separate neoplastic entity. Therefore, Ewing's tumor constitutes an intergradation with lymphoblastoma and myeloblastic tumors, on the one hand, and with fibrosarcoma and osteogenic sarcoma, on the other.

#### CONCLUSIONS

- 1. Ewing's tumor represents an arbitrary subdivision of malignant bone neoplasms. Histopathologically it cannot be considered a neoplastic entity.
- 2. Roentgen signs of Ewing's tumor are not unequivocally characteristic. They result from destructive and reparative processes in osseous tissue any of which may be seen in osteogenic sarcoma, metastatic tumor or non-neoplastic lesions.
- 3. Correlation of clinical, roentgenological and histopathological data is necessary in order to establish the correct diagnosis and proper classification of primary bone tumors.
- 4. Biopsy should be done as early as possible in any bone lesion where primary neoplasm is suspected.

#### REFERENCES

- Ewing, J. Review and classification of bone sarcoma. Arch. Surg., 1922, 4, 485. Endothelial myeloma of bone. Proc. New York Path. Soc., 1924, 24, 93.
- 2. COLVILLE, H. C., and WILLIS, R. A. Neuroblastoma metastases in bones, with criticism of Ewing's endothelioma. *Am. J. Path.*, 1933, 9, 421-430.
- 3. Rix, R. R., and Geschickter, C. F. Tumors of the spine, with consideration of Ewing's sarcoma. *Arch. Surg.*, 1938, 36, 899-948.
- 4. CONNOR, C. L. Endothelial myeloma, Ewing. Arch. Surg., 1926, 12, 789-829.
- GESCHICKTER, C. F., and COPELAND, M. M. Tumors of Bone. Second edition. American Journal of Cancer, New York, 1936.
- 6. Roome, N. W., and Delaney, P. A. Undifferentiated round-cell sarcoma of the ilium (Ewing tumor) containing hemopoietic elements. Am. J. Cancer, 1932, 16, 386–398.
- 7. Melnick, P. J. Histogenesis of Ewing's sarcoma of bone, with post-mortem report of case. *Am. J. Cancer*, 1933, 19, 353-363.

## QUIESCENT INTERVAL AND BONE METASTASES IN LYMPHOSARCOMA\*

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BOTH the duration of the quiescent interval and the frequency of occurrence of bone metastases seem significant factors in the prognosis of lymphosarcoma. Little attention seems to have been paid to either of these factors, however, except in special instances. The fact that the case here reported presented unusual features in both these respects has been responsible for a review of these aspects of lymphosarcoma.

#### LITERATURE

Regarding duration of the quiescent interval, Craver's¹ data in 96 cases show a total number of 7 cases (7 per cent) surviving for more than five years. The average survival since admission in this group of 7 cases is 7.3 years. Of Cutler's³ 16 cases in which death occurred, only 1 survived more than four years. Of the living patients in his series 4 out of 13 were alive after four years, while 2 others were alive after more than 5.5 years. Minot and Isaacs⁵ reported 1 patient well after six years.

Bone metastases in lymphosarcoma have received very little attention. As noted by Craver and Copeland<sup>2</sup> few if any reports of large series of cases provide information on this aspect of lymphosarcoma. In Craver and Copeland's series of 164 cases, 17 (10 per cent) had bone involvement. In cases with bone involvement the following characteristics were apparent. Metastases were noted from twenty days to one year prior to death. Most patients died before the end of the third year. Bone involvenent in order of frequency was spine, pelvis, skull, femur, humerus, tibia, scapıla, mandible, fibula, and ribs. Lesions in the bones were either osteoplastic or osteoytic, with the latter predominating. All he metastases originated from reticulum cell arcomas.

#### FEPORT OF CASE

T. E. D., a male, white, aged forty-eight, first noted the onset of generalized enlargement of the lymph nodes in August, 1932. Subsequently there was a slow, progressive increase in size so that in April, 1933, he consulted a physician. Upor examination at that time by

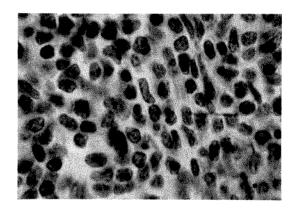


Fig. 1. Biops/ specimen inguinal lymph node, May 9, 1933.

Dr. H. D. Mesker, there were "numerous discrete nodules n each submaxillary space and in both carotid chains. There were small but palpable glands in both axillae and both groins." There was no elevation of temperature, no chest no- abdominal symptoms and a roentgenogram of the chest showed no enlargement of the mediastinal lymph nodes. On April 21, 1933, hemoglobin was 105 per cent, erythrocytes 5,600,000, and leukocytes 5,400. A differential count of the leukocytes showed 75 per cent polymorphonuclears, 24 per cent lymphocytes and 1 per cent eosinophiles.

Biopsy of two inguinal lymph nodes on May 9, 1933 (slides and reports furnished by Drs. H. D. Meeker and H. R. Muller) showed (Fig. 1) an overgrowth of small round cells such that the normal architecture of the lymph node was partially destrowed. No eosinophiles nor Dorothy Reed cells were present.

Following roeatgen treatment and a vacation

<sup>\*</sup> Read at the meeting of the American Association for the Study of Neoplastic Diseases, Washington, D. C., Sept. 10, 1937.

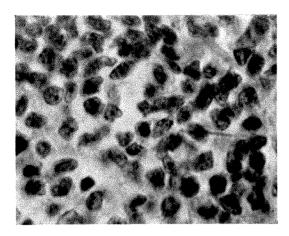


Fig. 2. Histological appearance o popliteal lymph node removed at biopsy April 12, 1937.

of six months in Florida, the patient remained well until December, 1936. At that time he was seen because of pain in the right chest. Following an evening of group singing he noticed a gradually increasing discomfort in the right chest, which discomfort at times felt like "gas pushing upwards" on the right side. He was unable to take a deep breath. Physical examination revealed a very slight icteric tinge to the skin, pale mucous membranes, and generalized glandular enlargements. All superficial lymph nodes were enlarged, particularly the axillary and left popliteal, these being approximately 2 cm. in diameter. Roentgenoscopic examination of the chest, together with roentgenograms, showed a marked widening of the mediastinal shadow, a thickened interlocar pleura and a slight increase in density in the lateral portion of the right lung in the region of the third, fourth and fifth ribs. Following a series of roentgen treatments the patient by January 22, 1937, reported that he was feeling well, breathing much better and that he could breathe without difficulty.

A second series of roentgenograms taken on February 9, 1937, showed a return to normal size of the mediastinal lymph nodes, disappearance of the interlobar thickening, but a persistence of the shadow in the lung.

Beginning on March 27, 1937, the patient experienced an upper restiratory infection which gradually increased in severity such that his temperature for several days reached 103° to 104° F. Cough was considerable and was accompanied by recurrence of pain in the right chest. This pain having increased, on April 12,

1937, the third series of roentgenograms was taken. Corresponding to a palpable mass 3 by 5 cm. was the area of increased density and the fracture of the rib. Physical examination at this time revealed barely palpable axillary and inguinal lymph nodes, non-palpable cervical, posterior-occipital and epitrochlear lymph nodes and the left popliteal lymph node 2 cm. in diameter. Temperature ranged around 99.2° F. A mass 15 by 20 cm. was palpable in the abdomen, near the umbilicus.

On April 12, 1937, biopsy of the left popliteal lymph node, which had received no roentgen treatment, was done. Histologically the tissue was composed entirely of small lymphocytes, some of which were seen in mitosis. There was some fibrosis but neither eosinophiles nor Dorothy Reed cells were present (Fig. 2). These findings were essentially the same as those of Meeker and Muller four years previously.

Following this, the patient received large doses of roentgen therapy to the abdominal mass. Even on May 27, 1937, he weighed 157 pounds, a loss of only 8 pounds from his maximal weight. The cough continued with slight remissions, fluid collected in the abdomen and he died on June 25. Autopsy was not obtained.

#### DISCUSSION

The present case is interesting from several standpoints. First is the relationship between histological appearance and the quiescent interval. The patient went for a period of four years without sufficient symptoms to necessitate consulting a physician or communicating with his physician who previously had made a definite diagnosis of lymphosarcoma from the biopsy.

In the literature, the "simple lymphomata," "lymphadenomata" or "hyperplastic lymphadenitis" cases are associated with long clinical courses. Le Count's case of this type continued for fifteen years, while one of Ewing's cases (Cutler continued for eighteen years, with fatal outcome. In none of these cases was there metastasis to bones while conversely in none of Craver and Copeland's cases with bone metastasis was the lymphosarcoma of the type reported. The histological appearance of the lymph nodes in the case

here reported, similar at both beginning and end of the disease, is that of a supposedly benign lymphatic tumor. Its metastasis to bone, previously reported as occurring only in the reticulum cell type of lymphoma, therefore is very unusual.

The metastic lesion in the rib was predominantly osteolytic in type. In one of Craver and Copeland's cases (their Case 5) "a lesion in a rib showed rarefaction without marked alteration in the structure of the bone," apparently without pathologic fracture.

As in most cases of bone involvement, attention was called to the rib metastasis by pain locally. It seems unusual that the rib metastasis became evident soon after such excellent response to roentgen treatment had been obtained upon the part of the mediastinal lymph nodes.

According to the frequency of occurrence, metastases of lymphosarcoma to ribs are very rare. Craver and Copeland, however, do state that bone involvement,

particularly of the vertebrae, occurs chiefly through expersion, and it is probable that the rib in the case here reported was involved in that fashion.

#### SUMMARY

A case of lymphosarcoma of round cell type with four years' quiescent period and metastasis  $\infty$  sone (rib) is reported.

#### REFERENCES

- 1. CRAVER, L. F. Five year survivals in lymphatic tumors. Szrg, Gynec. & Obst., 1935, 60, 485.
- 2. Craver, L. F., and Copeland, M. M. Lymphosarcoma in bone. Arch. Surg., 1934, 28, 809-824.
- 3. Cutler, M. Lymphosarcoma; clinical, pathologic and radiotmerapeutic study, with report of 30 cases. Arch. Szrg., 1935, 30, 405-441.
- LE COUNT, E. R. Lymphoma; a benign tumor representing a lymph gland in structure. J. Exper. Med., 189, 4, 559.
- 5. MINOT, G. R., and ISAACS, R. Lymphoblastoma (malignant lymphoma); age and sex incidence, duration of disease, and effect of roentgen-ray and radium irradiation and surgery. J. Am. M. Ass., 1926, 26, 185-1189; 1265-1270.



# INTRACRANIAL COMPLICATIONS FOLLOWING IRRADIATION FOR CARCINOMA OF THE SCALP\*

By EUGENE P. PENDERGRASS, M.D., PHILIP J. HODES, M.D., and ROBERT A. GROFF, M.D.

PHILADELPHIA, PENNSYLVANIA

WF. have observed fatal intracranial complications in 3 patients who received large doses of radiation for carcinoma of the scalp. The purpose of this communication is to call attention to the therapeutic procedures employed in these patients and to record their operative and post-mortem findings.

Fig. 1. Case 1. Note denuded sone in center of lesion at A. Photograph taken ir February, 1937.

Case 1. O. McH., male aged sixty, was admitted February 10, 1937, complaining of an ulcer of the scalp of eleven years' duration (Fig. 1). The lesion was first treated with radiation five years prior to his present admission. The quality and quantity of radiation employed were unknown though we believe low voltage rays were employed as the treatment was given by a dermatclogist. In November,

1935, the patient was again irradiated. During the following twelve months, the lesion was treated at various intervals with high voltage radiation (200 kv., 50 cm. skin-target distance), receiving a total of 5,000 r filtered through 0.50-0.75 mm. of copper (Fig. 2).

The patient was first seen in the Department of Radiology of the Hospital of the University of Pennsylvania on February 10, 1937. On ex-

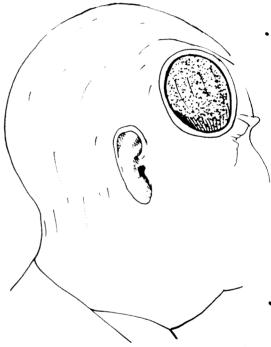


Fig. 2. Case 1. Treatment received in years prior to admission to Department of Radiology of Hospital of University of Pennsylvania, February, 1937. Before November, 1935: Superficial therapy, total dose and physical factors unknown.

November, 1935—November, 1937 November, 1935—1,000 r in 5 days (0.5 mm. Cu) March, 1936—1,600 r in 4 days (0.5 mm. Cu) September, 1936—2,000 r in 16 days (0.75 mm. Cu)

November, 1937—1,000 r in 7 days (0.75 mm. Cu)
Physical factors, 200 kv., 50 cm. skin-target distance.

<sup>\*</sup> From the Departments of Radiology and Neurosurgery of the Hospital of the University of Pennsylvania, Philadelphia. Read at the Thirty-Ninth Annual Meet ng, American Roentgen Ray Society, Atlantic City, N. J., Sept. 20–23, 1938.

amination, a foul, necrotic, sloughing ulcer (Fig. 1), 13 cm. in diameter, was found overlying the right frontal bone. The bone in the center of the involved area was denuded. The edges were raised with considerable infiltration evident in the outer canthus and upper lid of the right eye. No metastatic nodes were palpable in the cervical region.

Biopsy showed spinocellular carcinoma, Grade 2.

Laboratory Data. Blood chemistry and serology, negative.

Roentgen Examination. There was a demineralized area in the frontal bone on the right side due either to infection, malignant disease, or both.

Therapeutic Course. The patient received his first roentgen treatment from us on February 10, 1937. The entire lesion was divided into six fields, each 7 cm. in diameter (Fig. 3). One por-

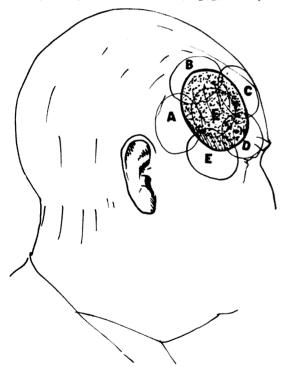


Fig. 3. Case 1. Treatment received February, 1937—March, 1937. Portals A, B, C, D, E, F, 7 cm. diameter, daily dose, 350 r to one area; total dose, 2,000 r×6; total treatment period, fifty-five days. Physical factors: oil-cooled air-insulated shockproof tube, constant potential generator, 200 kv. (peak), 15 ma. 3 per cent ripple, 18 cm. skin-target distance; 5 mm. Cu equivalent filtration (Thoraeus, 1.25 mm. tin, 0.25 mm. Cu, 1.0 mm. Al); 160 r per minute delivered to skin with these factors.

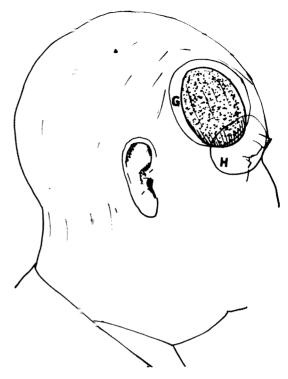


Fig. 4. Case 4. Treatment received April, 1937—May, 1937. Pertal G, 9 cm. diameter; daily dose, 400 r; total dose, 2,000 r; total treatment period, six days. Pertal H, 7 cm. diameter; daily dose, 400 r; total dose, 5,000 r; total treatment period, six days. Physical factors: Same as in Figure 3.

tal was treated daily, 350 r\* being delivered at each sitting. The rays were emitted by an oilcooled, air-insulated, shock-proof tube energized by a 200 kv. constant potential generator operating at 15 ma. (ripple 3 per cent). The target skin cistance was 18 cm. A Thoraeus filter equivalent to 5 mm. of copper (1.25 mm. tin, 0.25 mm Cu, 1.0 mm. Al) was employed, the afflux being 160 r a minute. The patient received 2,000 t to each of the six portals in fifty-five days which produced a moderately severe epithelitis exudativa. On April 12, 1937, two weeks after the last treatment, a biopsy revealed evidence of active malignancy. Following a consultation with another radiologist, the lesion was given an additional 2,000 r to each of two portals in six days (Fig. 4). Examination in June, 1937, revealed considerable slough in the center of the u.ce. with continued healing about its periphery.

Several days later, June 17, 1937, the patient complained of loss of control of the fingers of

<sup>\*</sup> r = in air without back-scatter.

his left hand. He was drowsy and complained of headache. A roentgen examination of the skull revealed no pineal shift. The bone demineralization previously reported had progressed though it was impossible to tell from the roentgenograms alone whether the bone changes were due to infection, n alignancy, or both. Because of these findings, the patient was hospitalized.

Following operation, the patient's headache subsided and the weakness of the arm and leg disappeared. A culture of the material obtained from the cavity in the brain showed both Staphylococcus albus, and Streptococcus haemolyticus.

Seven days after operation, the original clinical picture began to return, the patient developing left hemiparesis and stupor. The

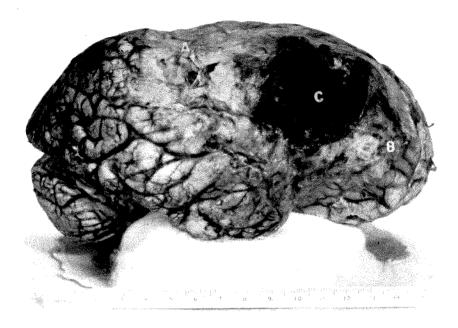


Fig. 5. Case 1. Right lateral view of brain showing the diffuse inflammatory reaction more marked at A and B. Area C is the site of the primary focus of infection where brain herniated into cranial defect.

Physical and Neurological Examination. Upon admission to the hospital, the patient's temperature was 102° F., pulse 80 and respirations 24. The blood pressure was 12\_/68. The edges of the ulcerated area of the scalp were inflamed and reddened. The right eyelid was edematous. The cranial nerves were essertially negative. The eyegrounds showed hazitess of the disc margins. The left arm and leg were weaker than the right and their reflexes were increased.

On June 17, 1937, a trepnine was made through the exposed bone over the lower portion of the motor area. The dura was white, thickened and did not pulsate. After opening the dura, a beefy-red arachneid was exposed. Upon inspection and manipulation, a large cavity was opened which contained yellow fluid with "strings" of exudate. A rubber tissue drain was inserted and dressir gs applied.

trephine was enlarged at a second operation by rongeur. The bone removed was dry and thin. It did not have the appearance of osteomyelitis. A foul-smelling, greenish exudate was present over the entire brain exposed. Degenerated brain substance was removed and adequate drainage obtained. The patient's condition was not altered. Two days after the second operation, the patient died.

Pathological Examination. At autopsy the brain, upon gross inspection, was covered by an extremely thick, milky, suppurative exudate (Fig. 5). The base of the brain and brain stem were likewise covered by this intense suppuration (Fig. 6). The ependymal lining of the lateral ventricles was covered by a thick white exudate. This was particularly heavy on the roofs of the anterior horns of the ventricles, attaining a thickness of almost 0.5 cm. This

thickening of the ependyma and suppurat ve exudate were also present in the third and fourth ventricles.

The vessels of the brain showed marked congestion and numerous hemorrhages were present throughout. The right half of the dura was thickened and revealed an internal suppurative process. A diagnosis of suppurative meningitis extending over the entire brain was made together with a thickening of and suppurative exudate over the entire ependyma of the lateral centricles.

Microscopic Description (Dr. B. J. Alpers). "There is a very thick exudate covering the cortex. The lower layers next to the cortex are composed of a dense fibrous exudate in which there are many lymphocytes and an occasional large mononuclear cell. The more superficial parts of the exudate are composed of polymorphonuclear leukocytes which lie in scattered strands of fibrin. The pial vessels are thickened and their walls infiltrated by leukocytes. The cortical vessels show swelling and proliferation of the endothelium. There is extensive infiltration of the brain tissue with leukocytes. Fresh hemorrhages are seen here and there. The ganglion cells are swollen. Co-

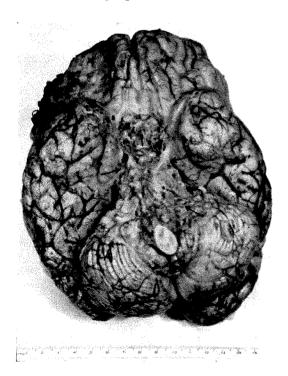


Fig. 6. Case 1. Base view of brain showing the marked basilar meningitis.



Fig. 7. Case 41. Note the denuded bone (arrow). Photograph taken in March, 1937.

lections of leak ocytes are present everywhere in the brain t ssue. *Diagnosis:* Meningo-encephalitis—purulent."

Summary of Case 1. The patient, aged sixty, received an unknown amount of low voltage rays for a cancer of the scalp five years prior to his present admission. High voltage radat on, 200 kv., was then directed to the lesion at irregular intervals for twelve months before the patient was first seen by us, the lesion receiving 5,000 r during this period. Two months later, the lesion received 2,000 r × 6 in fifty-five days of high voltage radiation in our department. The patient was given an additional 2,000 r to each of two portals three weeks later for evidence of residual malignancy. The patient developed evidence of an intracranial lezion six weeks after the last treatment. A dural and subdural infection was found and drained. The patient ultimately succarabed to the intracranial infection and died. A diffuse purulent meningo-encept alitis was found at autopsy.

Case II. H. B, male, aged fifty-three, was admitted Marth 27, 1937, complaining of an ulcer of the scalp of nine months' duration. During this time the lesion had been treated

with caustic salves applied locally without success. On examination, an ulceration in the scalp, to cm. in diameter, overlying the left parietal bone was found (Fig. 7). The edges were indurated and the entire area exaded pus. Several enlarged nodes in the posterior cervical chain suggested metastasis.

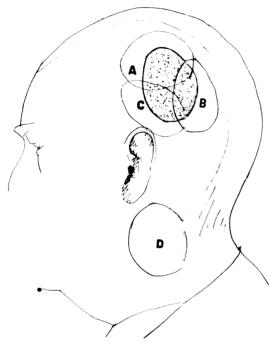


Fig. 8. Case II. Treatment received March, 1937—April, 1937. Portals A, B, C, 9 cm. diameter; daily dose, 400 r to one area; total dose, 2,100 r×3; total treatment period, sixteen days. Portal D, 9 cm. diameter; daily dose, 300 r [every other day); total dose, 2,800 r; total treatment period, fifteen days. Physical factors for portals A and B: Same as in Figure 3.

Biopsy showed squamous cell carcinoma, Grade 2.

Laboratory Data. Blood chemistry and serology, negative.

Roentgen Examination. The bones of the vault were negative.

Therapeutic Course. Treatment was started on March 30, 1937. The entire lesion was divided into three fields, each 9 cm. in diameter (Fig. 8). Another 9 cm. circular portal was directed into the metastatic cervical nodes. The lesion in the scalp was treated daily, 400 r being delivered through one portal per day. In addition, the metastatic nodes received 300 r at each sitting. The rays were emitted by an

oil-cooled, air-insulated, shock-proof tube activated by a 200 kv. constant potential generator operating at 15 ma. The target-skin distance was 18 cm. A Thoraeus filter equivalent to 5 mm. of copper (1.25 mm. tin, 0.25 mm. Cu, 1.0 mm. Al) was employed, the intensity being 160 r per minute. The patient received 2,100 r to each of the three portals over the skull in sixteen days. The metastatic nodes in the neck received 2,800 r in fifteen days.

The lesion in the skull developed a moderately severe epithelitis exudativa which began to heal in two weeks. The metastatic nodes became smaller and freely movable. On June 5, 1937, because of the marked improvement in the scalp lesion, burr holes were drilled into the denuded bone to hasten granulation tissue formation. At operation, the soft texture of the bone was noted. The metastatic nodes were surgically removed. Subsequently, these nodes proved to be invaded by squamous cell carcinoma.

On June 11, 1937, the patient began to have difficulty talking. Words were not pronounced correctly. This increased until the time of admission, when his speech was limited to one or two words. At about the same time, the right hand became clumsy, with some loss of motor power. The day before admission, the patient had a jacksonian convulsion on the right, becoming generalized before completion.

Physical and Neurological Examination. On admission, June 15, 1937, the patient was stuporous. The right arm was weak and there was a reduction of sensation over the right arm, right shoulder, and the right side of the neck. The patient had an aphasia which was almost complete. The eyegrounds showed early choking.

On June 15, 1937, a left occipitoparietal craniotomy was performed. Upon opening the dura, pus exuded from between the dura and brain. The location of the abscess was directly beneath the upper portion of the ulcerated scalp. Appropriate drainage was instituted. The pus culture revealed staphylococci.

Convalescence was slow. One week later, an exploration for a subcortical abscess was made but none found. Following this the power and stereognostic sense returned in the right arm and the aphasia cleared completely. The patient was discharged from the hospital on June 24, 1937.

The patient was readmitted July 7, 1937, because of hemorrhage which had occurred from

under the ulcerated scalp edge. Examination did not reveal the source of hemorrhage and after two days' observation, the patient was discharged.

Five days after discharge, the aphasia and weakness of the right hand and arm returned. On July 10, he was readmitted to the hospital. Two days later, the bone flap was removed together with some cerebral tissue beneath the cranial defect. This tissue, on histological examination, proved to contain evidences of a

process extended into the substance of the brain for a distance of 3 cm. In the right anterior portion of the first temporal convolution, 1 cm. below the surface of the cortex, there was a round, apparently encapsulated tumor mass measuring 1 cm. in diameter (Fig. 10).

Microscopic Description of Brain (Dr. B. J. Alpers). "There are two types of tissue reaction: (1) a vascular process, and (2) a tumor.

Vascular process: In the right hemisphere beneath the ulterated scalp lesion is a definite

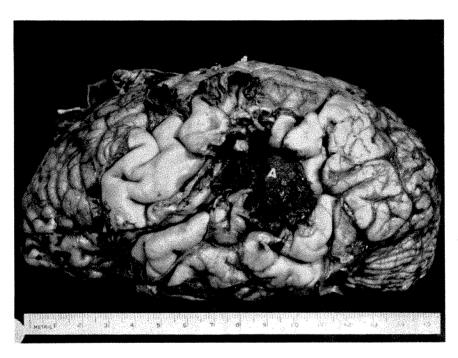


Fig. 9. Case II. Left lateral view of brain. A shows the degenerated and offened area, the result of vascular occlusion. This area occurred directly beneath the scalp lesion.

low grade infection and fresh hemorrhage. Following the removal of the bone flap, a cerebral fungus—herniation—developed and in this state, the patient continued until August 22, when he developed bronchopneumonia and died.

Gross Description of Brain. Except for a hard hemorrhagic area beneath the cranial defect on the left side in the region of the angular gyrus and widening of the surrounding gyri, there was nothing of note to be seen on gross inspection of the brain (Fig. 9).

Coronal sections of the brain were made after it had hardened properly (Fig. 10). A section through the hard hemorrhagic area in the region of the left angular gyrus disclosed that the

pathological process. This is characterized by changes in the ressels and in the surrounding brain tissue. The middle cerebral artery shows almost a complese obliteration of its lumen due to internal proliteration. There has been canalization of this process. The proliferated tissue is fibroblastic. There is no evidence of inflammation within i. The elastica is broken in many pieces. There is no adventitial reaction either inflammatery or otherwise. A few of the other vessels show beginning internal changes. The brain tissue shows softening, with numerous gitter cells. These is also much fibrosis and gliosis in the tissue with formation of a capsule. Vessel proliferation a also seen. Areas of glial proliferation are aumerous. These are chiefly

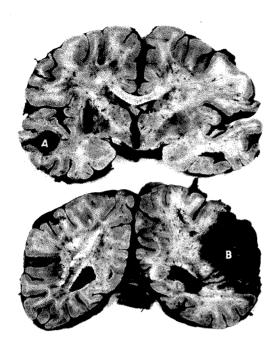


Fig. 10. Case 11. Coronal sections of brain. The metastatic nodule is shown at  $\mathcal{A}$ . The degenerated area is seen at  $\mathcal{B}$ .

astrocyfes. Lymphocytes and plasma cells are found in large numbers in these areas. Vessel proliferation is found in large numbers. *Diagnosis*: (1) metastatic carcinoma; (2) endarteritis; (3) old softening.

"Tumor: In the left temporal lobe, there is a tumor nodule which is clearly defined but which has no capsule. It extends into the brain tissue slightly. It is composed of large numbers of cells. These have a round, large, roomy cytoplasm which takes a pale acid stain which is frequently filled with vacuoles. The nucleus shows a marked degree of metamorphosis. Its shape varies so widely as to be indescribable. It has all sorts of shapes; it is often multiple, with cytoplasmic bridges connecting the various parts. It is heavily chromaticized and contains many vacuoles of varying sizes and numbers. Amitotic division is frequently seen. Mitoses are seen occasionally. There are many large sinuses within the tumor but very little connective tissue. The surrounding brain tissue shows very little."

Summary of Case 11. The patient, a male, aged fifty-three, received 2,100 r to each of three areas directed into a squamous

cell carcinoma of the scalp in sixteen days. Several metastatic cervical nodes were also treated. The nodes were subsequently excised and contained carcinoma. The lesion regressed rapidly. Burr holes were drilled into the calvarium to hasten granulation tissue proliferation. Eight weeks after the last treatment, signs of an intracranial infection developed. A subdural abscess was drained but the patient died. At autopsy, a large abscess was found in the brain. Even more unusual, was a sizable metastatic nodule in the contralateral temporal lobe. The metastatic foci in the cervical nodes and brain merit special comment as we have never observed similar metastases in patients with carcinoma of the scalp.

Case III. T. B., male, aged forty-seven, was admitted April 12, 1930, complaining of an ulcer of the scalp of nine years' duration. During these years, the lesion had been treated with bland ointments, caustics, desiccants, and roentgen rays without success.

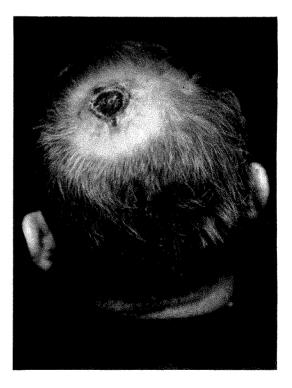


Fig. 11. Case III. Photograph taken February, 1932, before the lesion was desiccated.

On examination, an annular lesion, 4 cm. in diameter, was found overlying the parieto-occipital region (Fig. 11). The bone was not exposed.

Biopsy showed a basal cell carcinoma.

Laboratory Data. Blood chemistry and serology, negative.

Therapeutic Course. On April 12, 1930, the lesion was treated by means of ten radium tubes filtered through 0.3 mm. of allow metal. The total amount of radium contained in these tubes was 150 mg., the lesion being given 270 mg-hr. of radium in one hour forty-eight minutes (contact). The area healed completely in seven weeks. One year later, April 17, 1931, three recurrent nodules were noted in the margin of the scar. The area was again treated by means of three 100 mg. radium tubes contained in applicators with a wall thickness of 2 mm. of brass placed in contact with the skin, the lesion receiving 150 mg-hr. X3 in one and a half hours. On June 16, 1931, the area was again treated by means of radium for recurrence. Two 50 mg. and four 100 mg. radium cells filtered through 0.3 mm. of alloy metal were employed in contact with the skin. The 50 mg. applicators were applied for thirty-five minutes and the 100 mg. applicators for seventy minutes, delivering a dose of 29 mg-hr. X2 and 115 mg-hr. X4, respectively. On September 30 and October 1, 1931, the carcinoma was again treated. Thirteen radium tubes each containing 50 mg. of radium filtered through 2 mm. of brass were employed at a distance of 0.5 cm. Nine portals were treated, each receiving a total of 200 mg-hr. of radium. The reaction was severe but the lesion failed to disappear completely. On February 11, 1932, the bone was denuded with an endotherm knife (Fig. 13). Healing was rapid and complete. Several months later, the denuded bone was spotted with burr holes to promote granulation tissue proliferation. Roentgen examination of the skull in March, 1933, revealed a localized area of bone destruction in the region of the burr holes. The rarefied area was well circumscribed. The inner table of the skull was intact.

In July, 1933, biopsy from a suspicious margin of the lesion revealed basal cell carcinoma. The patient then received 5,000 r of unfiltered radiation and 2,600 r filtered through 0.25 mm. Cu in four days, July 21 to 24, 1933. The rays employed were emitted by an air-cooled, mechanically rectified unit operating at 135 ky.,

5 ma. The target skin distance was 30 cm., field 9 cm. in diameter, afflux being 100 r a minute for unfiltered radiation and 25 r a minute for 0.25 mm. Cu plus 1 mm. Al. In November, 1933, another biopsy proved positive and an additional 7,000 r of unfiltered radiation and 1,200 r with 1 mm. Al were delivered to the

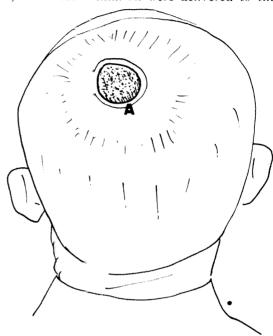


Fig. 12. Case III. Treatment prior to admission to Department of Radiology, April, 1930, ointments, desiccants, caustics, irradiation. Treatment received in our department April, 1930-April, 1933:

#### Portal A

April, 1930—17 mg-hr. ×10 radium (0.3 mm. alloy, contact, hr. 45 min.)

April, 1931—130 mg-hr. ×3 radium (2 mm. brass, contact, 1 hr. 30 min.)

June, 1931—29 mg-hr. ×2 radium and 115 mg-hr. ×4 radium (#.3 mm. alloy, contact, 35 min.)

×4 radium (= 3 mm. alloy, contact, 35 min.) September, 193 = 200 mg-hr.×9 radium (2 mm.

brass, 0.5 cm. distance, 5 hr. 10 min.) February, 1932—e ectrothermic resection.

March, 1933—bur: holes drilled into calvarium.

lesion on December 4 to 5, 1933. Roentgen examination of the head at this time revealed no change in the characteristics of the bone defect since the examination in March, 1933.

In February, 1934, the denuded bone began to suppurate. A soul-smelling osteomyelitis rapidly developed which was treated with maggots in April, 1934. In May, 1934, the patient began to develop signs of an intracranial

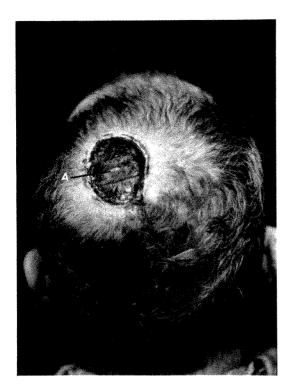


Fig. 13. Case III. Photograph taken February, 1932, after electrothermic removal of the basal cell carcinoma. Note the denuded bone at A.

lesion. An extradural abscess was exposed and drained. The bone continued to sequestrate. In June, 1934, the bone was completely destroyed allowing the dura to bulge into the wound and break down.

The dura eventually degenerated, the brain lying exposed in the infected alcer bed. The patient died shortly thereafter of a diffuse streptococcic meningitis. A post-mortem examination was not permitted.

Summary of Case 111. The patient, a male, aged forty-seven, received 2,750 mg-hr. of radium in eighteen months to a basal cell carcinoma of the scalp (Fig. 12). Later, a recurrence was removed surgically leaving denuded bone. The bone was subsequently spotted with burn holes to promote granulation tissue proliferation. Another recurrence developed which received 15,200 r of low voltage radiation in five months (Fig. 14). Osteomyelitis of the calvarium developed which progressed until a large portion of the dura became exposed.

The dura and brain subsequently degenerated. A diffuse streptococcic meningitis caused death. Autopsy was not obtained.

#### COMMENT

The intracranial symptoms which developed in the patients being reported were those of increased intracranial pressure—namely, choked discs, stupor, and headache. The focal signs and symptoms were referable to the portion of the brain beneath the scalp lesion. Case I died of a purulent meningo-encephalitis. Case III died of a streptococcic meningitis. Both patients received large quantities of radiation over a period of years. Case II was given the smallest amount of radiation. Death in this patient was due to an obliterative endarteritis and brain softening. In each

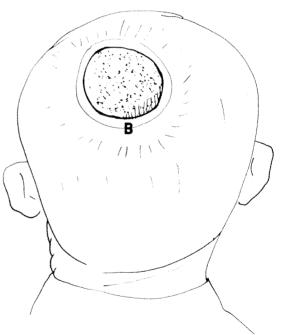


Fig. 14. Case III. Treatment received July, 1933–November, 1933: Portal B: July, 1933, 5,000 r in four days (unfiltered); 2,600 r in four days (0.25 mm. Cu); November, 1933, 7,000 r in two days (unfiltered); 1,200 r in two days (1.0 mm. Al). Physical factors: air-cooled nonshock-proof tube, mechanical rectifier; 130 kv., 5 ma., 30 cm. skin-target distance; 100 r per minute delivered to skin with these factors, unfiltered; 25 r per minute delivered to skin with these factors (0.25 mm. Cu plus 1 mm. Al).

instance, the first craniectomy revealed a focal subdural abscess. In Case 1 and Case, 11 the abscess developed at six and eight week intervals following irradiation. The abscess in Case 111 developed six months after irradiation.

Extensive carcinomas of the scalp are frequently associated with bone changes attributable to infection, malignant disease, or a combination of both. It is often impossible to distinguish between these destructive processes. Under such circumstances, the clinical findings are of paramount significance. When infected, the cranium logses its shiny, glistening appearance, becoming dull, gray or gravish-black and porous. Sometimes, the bone seems to "weep" droplets of pus as it oozes from the haversian canals. All of our patients presented these clinical signs. Roentgen evidences of infection were demonstrable in Case I and Case III. In Case II, the denuded and infected bone appeared normal roentgenographically. The difference in the clinical and roentgen observations in this patient is not unusual. Roentgen manifestations of infection frequently develop much later than the clinical signs. Roentgenographic evidences of malignant bone invasion occur still later.

The therapeutic procedures varied in each individual. One patient, Case II, had high voltage radiation (200 kv.) alone. Another, Case I, received intermediate voltage (135 kv.) and high voltage (200 kv.) radiation. The third patient, Case III, was treated with radium and intermediate voltage (135 kv.) rays. The total dose employed in each instance varied considerably. In spite of these differences, each patient died of an intracranial infection.

# DISCUSSION

A review of the literature pertaining to the treatment of carcinoma of the scalp throws little light upon the development of the intracranial infections observed above. Though bone infections and necrosis have been reported<sup>3,5,7</sup> following irradiation of the calvarium, we could find nothing simu-

lating the complications encountered in our patients. Conferences with colleagues<sup>10</sup> also failed to reveal similar experiences, though comparable doses of radiation were being employed for scalp cancers in the presence of infected and denuded bone. According to these men their results, in lesions similar to the ones we treated, were uniformly good irrespective of the type of therapy employed.

For years these lesions were successfully handled in our hospital by a combination of irradiation plus wide desiccation. By this method the pericranium and bone were purposely destroyed. Subsequently, covering of the exposed bone was facilitated by burr holes which stimulated granulation tissue proliferation and healing. Because such methods seemed extreme, we hoped that carcinolytic doses of radiation might prove equally successful and less mutilating. In view of past experiences in treating patients with brain tumors, we felt no hesitancy in exposing the head to large quantities of radiation. By decreasing the target-skin distance to 18 cm., we hoped to protect the bone and brain still further, and at the same time to increase the absorption of radiation in the superficial tissues. In view of past experiences with in fections following the combined method for treating carcinomas of the scalp, no unusual methods for controlling infection seemed necessary.

We are not prepared to answer the question as to why our patients developed intracranial infections. Certain observations in the literature relative to this problem, however, seem to merit discussion.

Ewing<sup>4</sup> has called attention to the peculiar susceptibility of the blood vascular system of bone to strangulation by irradiation. That such changes render membranous bone unusually fertile soil for bacterial invasion and necrosis has been amply demonstrated.<sup>1,2,4,8,11</sup> One patient in our group, Case III, developed bone necrosis. All three, however, had clinical, operative and histologic evidence of bone infection.

Normally, the spread of infections in the



Fig. 15. Case 11. Section of bone showing, in the haversian canal, the presence of an inflammatory reaction at B with connective tissue formation and a vessel which is occluded. The vessel wall is distinctly thickened showing evidence of previous phlebitis at A.

body is limited by inherent protective mechanisms of the host. Most men agree that small doses of radiation enhance these protective forces. Large doses, however, impede rather than support them. It seems reasonable to believe, therefore, that the carcinolytic doses of radiation employed in our patients produced enough destruction of the normal immunologic barriers to infection to allow the spread of infection from the cranium by re-rograde thrombophlebitis (Fig. 15). The meninges becoming infected, few barriers remained to prevent extension into the intracranial tissues. It is of interest to note that the most severe infections occurred in those patients (Cases I and III) who received the greatest amount of radiation. It is only fair to state, however, that both these patients had streptococcic infections whereas the third individual (Case II) had a staphylococcic infection which remained localized.

In the light of recent experiences, the brain can no longer be considered insensitive to radiation. Reflex changes, 6,9 cere-

bral hypoplasia, vascular changes and glial degeneration reported in the literature bear ample testimony to this fact. The question arises, therefore, were the brain changes observed in our patients due to irradiation plus secondary infection? We have been assured by Dr. B. J. Alpers that the findings were primarily due to infection with little evidence present to suggest brain degeneration of the type seen following irradiation.

From the above experiences and observations, the question arises as to what should be the method of choice in the treatment of large carcinomas of the scalp. Does irradiation have a place in the treatment of this form of malignancy? If so, how should the problem of infection be handled? Or is. surgery, either by electrothermic methods or scalpel, the safest procedure? We do not know the answer to the problem. We would hesitate, however, to employ irradiation in the manner described above without warning the patient's family as to the seriousness of possible complications. We believe more care should be exercised to control infection. We do not believe burr holes should be made into denuded cranial bones until all evidences of infection have been lacking for months.

#### SUMMARY

- 1. We have reported three patients with carcinoma of the scalp who died following irradiation.
- 2. In each instance, the fatal complication occurred as the result of an intracranial infection.
- 3. Complete post-mortem studies in two cases have been recorded.

### REFERENCES

- I. COLWELL, H. A., and Russ, S. X-Ray and Radium Injuries. Oxford University Press, New York and London, 1934, pp. 151-159.
- 2. Desjardins, A. U. Osteogenic tumor: growth injury of bone and muscular atrophy following therapeutic irradiation. *Radiology*, 1930, 14, 296-308.
- 3. ELSBERG, C. A., DAVIDOFF, L. M., and DYKE, C. G. Roentgen treatment of tumors of brain

- in operating room by direct radiation through open wound. Bull. Neurol. Inst. New York, 1937, 6, 19-32.
- 4. Ewing, J. Radiation osteitis. Acta radiol., 1926, 6, 399-412.
- MARKIEWICZ, T. Late injuries to human brain due to roentgen irradiation. Ztschr. f. d. ges. Neurol. u. Psychiat., 1935, 152, 548-568.
- Nemenow, M. I. Effect of roentgen-ray exposures of cerebral cortex on activity of cerebral hemispheres. *Radiology*, 1934, 23, 86-93.
- 7. New, G. B., Figi, F. A., and Havens, F. Z. Replacement of tissues of forehead and scalp. Surg. Clin. North America, 1934, 14, 607-613.
- REGAUD, C. Sur la sensibilité du tissu osseux normal vis-à-vis des radiations X et γ et sur le mécanisme de l'ostéo-radionécrose. Compt. rend. Soc. de biol., 1922, 87, 629-632.
- Scholz, W. Sensitiveness of brain to roentgen and radium rays. Klin. Wchnschr., 1935, I<sub>4</sub>, 189-193.
- 10. WIDMANN, B. P. Personal communication.
- 11. WIDMANN, B. P., and GILBERT, P. D. Bone necrosis related to irradiation. To be published in Am. J. Roentgenol. & Rad. Therapy.

#### DISCUSSION

Dr. Cornelius G. Dyke, New York City. I have enjoyed listening to this paper and it is very timely that the authors call attention to these 3 cases. Of course, it is extremely difficult to be certain that the irradiation had something to do with and was causative in producing death in their patients by an infectious process, but I have also encountered some clinical and experimental material that leads me to believe that radiation when given in large doses may decrease the resistance of the tissues.

We have had several patients who during the roentgen treatment of a glioma developed an epidural abscess several weeks or months after the operation. In addition to these cases, we have experimented and treated 31 patients in the operating room with rather large doses of roentgen rays delivered at one sitting. These patients received from 2,000 to 3,000 r, 200 kv. (peak), which was rather intensive radio-

therapy. Five of these 31 patients died of infections. That number is altogether too great for a hospital in which good aseptic technique is used and a large amount of brain surgery is done.

In addition to those 5 patients, a number of monkeys were irradiated with fairly large doses of roemitgen rays, and 3 out of 10 monkeys developed infections and died of meningitis or cerebral absress.

Therefore, from these various experiences, my feeling is that radiation in large doses apparently does interfere with the normal protective processes in the body and that some patients so treated are probably a bit more liable to infection and to succumb thereto than if they had not been treated in this manner.

I have one slide I would like to show (slide). When giving loses around 1,500 to 2,500 r in a rather short period of time, it is also well to remember that over a number of years this may have a definite effect on the brain. For instance, here is a slide showing the brain of a patient which had received 80 or 90 H.E.D. over a period of years. This patient from Berlin, reported by Markiewicz, subsequently developed blindness, convulsive attacks, and also had a large ulcer in the scalp and necrosis of the occipital bone. When this patient came to autopsy, I think t was somewhere in the neighborhood of four years after the last roentgen treatment was given, the medulla, and occipital and parietal lobes of the brain showed hemorrhagic necroses. Within the areas of necroses there were decreased reactions of the interstitial tissue and a deposit of homogeneous substances was noted which corresponded to Aizheimer's "coloid degeneration." The effects of irradiation on the brain, therefore, may become manifest five to fifteen years after treatment and prove fatal. A number of monkeys which were irradiated at the Neurological Institute did not show any immediate effect but later on did develop evidence of degenerative changes in the brain.



# WEAK RADIUM NEEDLE TECHNIQUE IN CARCINOMA OF THE CHEEK\*

By CHARLES L. MARTIN, E.E., M.D., F.A.C.R. DALLAS, TEXAS

THE interesting reports of Cade¹ and his associates from the Westminster Hospital in London, published some ten years ago, caused us to become interested in the use of needles containing very small amounts of radium as a substitute for radon seeds. A description of the first two needles adopted together with their advantages and disadvantages was published in 1932² and the three sizes which have

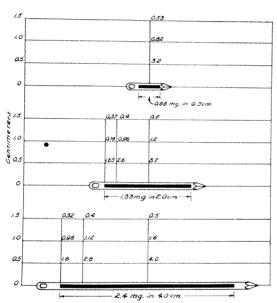


Fig. 1. Chart indicating effective threshold erythema doses at various distances from the weak radium needles when they are left in the tissues for seven days (168 hours).

been used for the past six years were described in 1935.<sup>3</sup> These needles have active lengths of 0.5, 2.0 and 4.0 cm. The small one contains 0.6 mg. of radium and the others contain 0.6 mg. per centimeter of active length. This type of loading was adopted because the reports of the British workers indicated that such needles placed parallel

to one another at 1.0 cm. intervals in epidermoid carcinoma in the mouth for seven days should produce a complete regression of the disease. At first it seemed only necessary to place them around the periphery of the tumor and some excellent regressions were produced in this manner, but since in most instances these regressions were not permanent, it became evident that a better distribution should be worked out. Much of our earlier work was done on an empirical basis, but figures published by Quimby4 in 1935 have helped us to rationalize our procedures. Although larger masses have been handled successfully this paper will be limited to a discussion of flat lesions having a thickness of 1.0 cm. or less. Such tumors are frequently encountered on the mucosa of the cheek, floor of the mouth, palate, lip and face. When thick polypoid masses are encountered, the projecting portions are removed with a radio knife loop so that the remaining tumor has the proper thickness. Early observations indicated that the best results followed the implantation of parallel needles into the base of the neoplasm so arranged that the active portions extended well outside its borders. In most instances extra needles were implanted in normal tissue outside the edges of the tumor. Such patterns made it impossible to use the tumor volume calculations proposed by Martin and Quimby<sup>5</sup> because the sources of radiant energy were not entirely within the malignant tissue.

Quimby has recently suggested that we depend entirely on point determinations in our work using her tables for needles of various lengths published in 1935. The chart shown in Figure 1 was constructed from these tables with some minor correc-

<sup>\*</sup> Read at the Twenty-Fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.

tions recently suggested by Quimby. The figures above each needle represent the number of threshold erythema doses delivered in the tissues at the locations incicated when the needles remain in position for 168 hours (seven days) which we have adopted as our standard time of treatment.

The data supplied by this chart can be used quickly and no elaborate calculations are necessary. The pattern used for a tumor measuring 4.0×1.5 cm. is shown in Figure 2 where only 2.0 cm. needles are used. At the point A the total radiation from the adjoining needles is  $3.7 \times 2$  or 7.4 threshold erythema doses. The needles placed 1.5 cm. from this point each furnish 0.5 T.E.D. or a total of 1.0 T.E.D. The more distant meedles deliver so little radiation that they can be neglected. The combined effect therefore amounts to 8.4 T.E.D. It is evident that with such an arrangement, the least radiation is delivered along the lower and upper edges and for this reason we have found it wise in some instances to place long needles at right angles to those shown in the sketch just above the heads and below the points. Such a plan delivers a dose of 7 to 8 T.E.D. fairly evenly throughout the tumor and the effective radiation falls within the range advocated as curative by Martin and Sharp<sup>6</sup> for intraoral lesions.

In our original article it was contended that the weak needles were more efficient than radon seeds used in accordance with the plan described by Martin and Sharp and the above calculations seem to bear this out. In Figure 2 the total amount of radium used amounts to almost 8.0 mg., whereas the above authors advocate 20.0 mc. as the amount of radon needed to deliver 7 T.E.D. to a tumor having a long diameter of 4.0 cm.

Although our experience with radon seeds is limited, we are led to believe that our plan is less likely to produce sloughing and bone damage because the active sources are spread out over a much larger area and in the near future we plan to publish statistics giving the incidence of these complications in our clinic.

It must be admitted that the technique of implanting and anchoring needles properly in the mouth constitutes one of the greatest objections to the method and some skill must be acquired before satisfactory patterns can be placed in the more irregu-

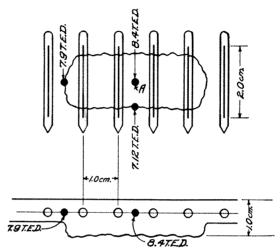


Fig. 2. Drawing illustrating the distribution of 1.33 mg. needles for the treatment of a tumor measuring 4.0×1.5 cm. The tissue dose averages from 7 to 8 T.E.D. throughout the tumor and the total amount of radium used is 8.0 mg.

lar lesions. This has been forcibly impressed on us through observing the awkwardness of surgical interns when they first become radiological residents. Fortunately, the needles can be removed and replaced until they are satisfactorily arranged and this in itself constitutes an advantage over the radon seed technique unless one uses removable seeds.

A needle of each type and the instruments employed in intraoral work are illustrated in Figure 3. The needles are placed in pure carbolic acid for ten minutes and then transferred to 70 per cent alcohol. They are then threaded with dental floss sutures which are tied in the middle so as to leave the two ends free and are returned to the alcohol for at least an hour before they are used. The hands of the technician who prepares the needles are scrubbed and sterilized before this procedure is carried out. The dental floss is obtained on 150 yard spools which have been sterilized and

placed in closed bottles. This suture material is quite strong and since it is waxed it does not tangle easily and is tolerated well by the tissues of the mouth. A sterile solution of butyn and epinephrine furnished in 4 oz. bottles keeps indefinitely

threaded into the eye of one of the small curved skin needles and a stitch is taken through normal mucous membrane and tied. The knot is always tied on the side of the stitch toward the needle and the long end of the suture is brought out through

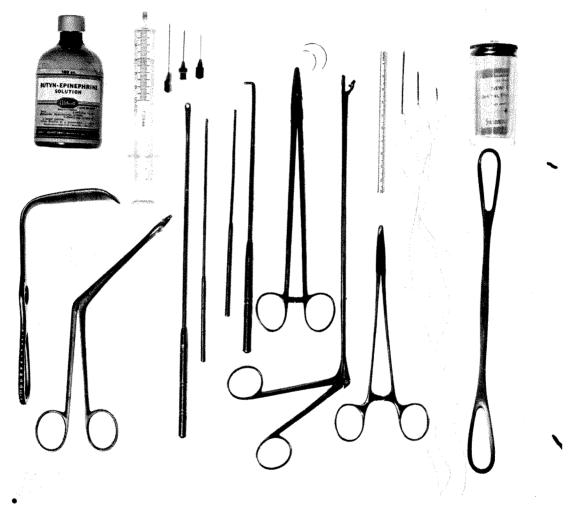


Fig. 3. Weak radium needles of each type threaded for use, anesthetic, demtal floss and instruments utilized in intraoral work.

and produces an excellent local anesthesia for intraoral work. Since any amount can be withdrawn through the rubber stopper in the bottle as it is needed, none of the solution need be wasted. After each needle is inserted with the heary forceps and forced below the surface with a countersinking instrument, the short end of the suture is

the corner of the mouth so that it may be tied into a tag attached to the forehead after the work is completed. When the knot is properly placed it is only necessary to cut the stitch on the side away from the knot to assure the easy removal of the needle by means of the long end of the suture. An instrument consisting of a bar with a

Y-shaped lower end has been found very useful in placing knots on the base of the tongue, in the soft palate, the anterior pillar and other locations not readily accessible to the operator's fingers. A pair of sewing forceps with a hole in the top of one jaw through which the curved needle may be passed greatly facilitates the placing of stitches in locations which are difficult of access. The long instrument with a round hole in its lower end is sometimes used in removing needles inserted in the back of the mouth with the points extending in an anterior direction. By threading the long suture through the hole and placing the end of the instrument in the throat, the tension on the thread can be exerted in a line parallel to the long axis of the needle. The biopsy forceps illustrated in Figure 3 have proved valuable because they possess very sharp cutting surfaces which make it possible to remove a fairly large specimen quickly. The resulting wound is immediately coagulated with a high frequency electrode and the field is free of hemorrhage during the implantation procedure. Since the care of the patient with radium needles in the mouth has been discussed in another article3 it will not be considered here.

#### CANCER OF THE CHEEK

The weak needles have been used with considerable success in cancer of the skin, tongue, palate, parotid, vulva, vagina and cervix, but cancer of the cheek has been selected to illustrate the results obtained because it constitutes the most common as well as the most favorable intraoral carcinoma seen in our clinic. The frequency of occurrence is probably due to the prevalence of "snuff dipping" among the women and tobacco chewing among the men in the rural districts of the Southwestern States. Martin and Pflueger<sup>7</sup> have described the poor results obtained in the treatment of cancer of the cheek with surgery alone and have collected a series of 79 cases reported by Warren, Brewer, Bradfield and Davis in which not a single operative cure was obtained. The reader is referred to this article for a survey of the rather scanty surgical literature.

Our first case was treated in 1930 and a survey of the 35 patients treated from 1930 to 1936, inclusive, is shown in Table 1. All stages of the disease are included and for that reason the results cannot honestly be compared with those obtained in operable

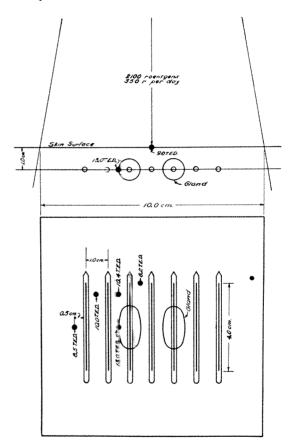


Fig. 4. Drawing illustrating the combined use of roentgen rays and weak radium needles used simultaneously for seven days in the treatment of the cervical lymphatic area when glarefular metastases have appeared. The effective dose varies from 10 to 13 T.E.D.

cases alone. Several changes in technique have been made and the more recent results are apparently much better than those obtained in the beginning. At first complete reliance was not placed on the implanted needles and several erythema doses were added using radium capsules held against the mucosa by means of lead strips.



Fig. 5. Three cases of proved carcinoma of the cheek which have remained well and free of cancer for six years following the use of weak radium needles. They are Cases xv, xiv, and ix reading from above as listed in Table 1. The lower case was an epidermoid carcinoma, Grade 2, and the others were both epidermoid carcinomas, Grade 1.

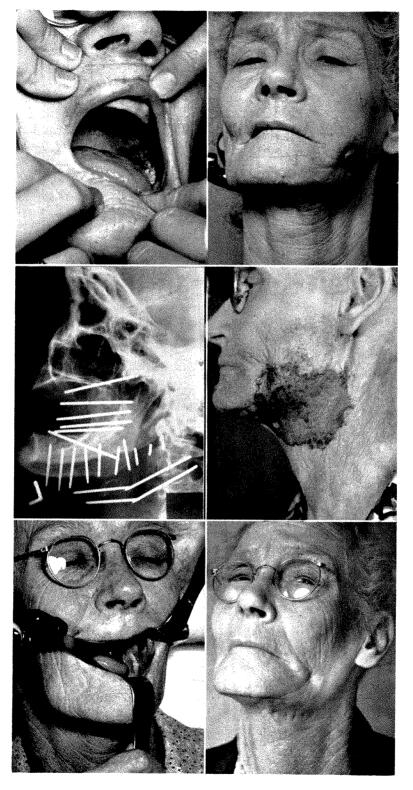


Fig. 6. Large epidermoid carcinoma, Grade 1, of cheek with perforation and mult ple submental and submaxillary lymph nodes treated with the combined radium needle implantation and roentgen therapy illustrated in Figure 4. The epithelitis healed rapidly and the lower photographs reveal no visible or palpable evidence of carcinoma seven months after the treatment was given.

		Primary Lesion			Tre	Treatment	
Case	Size cm.	Location	Pathology	Extension	Interstitial7 days	External	Results
1. D.S.C.	2.0	Mid cheek	Epidermoid cancer, Grade 2	No glands	7-0.6 mg. needles	1100 mg-hr. pack 600 r x-ray	Well 9 yr.
н. Ј.Б.С.	3.5	Gingiva and cheek	Epidermoid cancer, Grade 3	2 Submax, glands	10-0.6 mg. needles (\$20 mg.hr. contact)	1100 mg-hr. pack 2 areas	Local healing, glands growing at 5 mo.
m. J.W.D.	2.5	Gingiva and cheek		No glands	6-0.6 mg. needles	облиць 1111 готовиравания принципальной проформации подобрати	Untraced
FT RFH	2.0	Gingiva and cheek	Epidermoid cancer, Grade 3	No glands	9-0.6 mg. needles	NAPO, Aud M. prim prima para e para persona ministra de la republica de la descripción de la definidad de la r	Extension into jaw at 2 mo.
v. J.A.S.	2.3	Gingiva and cheek	Eddikingid concer no grade	No glands	9-0.6 mg. needles	2400 mg-hr. pack	Submax. glands 8 mo. later
vi. W.B.G.	6.0	Entire cheek	Epidermoid cancer, no grade	Latge submax, gland	8-41-33 cheek 7-10-6 4-1-33 gland	ogo mg-hr. pack boo r X-tuy	Local healing, died of recurrence 10 mo.
vii. C.C.M.	3.5	Carcinoma mouth, cheek and nose	Epidermoid cancer, Grade 2	No glands	11-0.6 mg. needles 11.33 mg. needles	600 r x-ray	Local healing, died 1 yr. later
viii. Mrs. T.P.R.	0.0	Entire cheek	Epidermoid cancer, Grade 2	No glands	9—1.33 mg. needles 8—0.6 mg. needles	3000 mg-hr. pack 300 r×6, each side	Local healing, deep recurrence in 10 mo.
IX. W.L.N.	3.5	Gingiva and cheek	Epidermoid cancer, Grade 2	Small glands?	16-0.6 mg. needles 7-1.33 mg. needles	3000 mg-hr. pack 600 r x-ray	Well 64 yr.
x. T.F.	50 10	Gingiva and cheek	Epidermoid cancer; no grade	I submax, gland	12-0.6 mouth 4-1.33 gland (300 mg-hr. contact)	2400 mg-hr. pack 600 r x-ray	Local healing, died 5 yr. later, recurrence
xı. J.M.P.	3.0	Gingiva and cheek with perforation	Epidermoid cancer, Grade 1	Large submax, gland	8—o.6 mg. needles 2—1.33 mg. needles	3000 mg-hr. pack 600 r x-ray	Temporary regression, died with deep re- currence
xn. D.J.S.	2.5	Gingiva and cheek	Epidermoid cancer, no grade	No glands	roo.6 mg. needles	To jaw 300 r×11	Local healing, recurrence in neck at 6 mo
хиг. Ј.С.N.	0.50	Whole cheek with perforation	Epidermoid cancer, Grade 2	No glands	4—0.6 mg. needles 11—1.33 mg. needles	3000 mg-hr. pack 600 r x-ray	Large clean hole in cheek at 8 mo., un- traced since
XIV. M.A.F.	5.	Lower cheek with perforation	Epidermoid cancer, Grade 1	No glands	9—0.6 mg. needles 1—1.33 mg. needles 2—2.4 mg. needles	3100 mg-hr. pack 600 r x-ray	Well 6 yr.
xv. W.A.Y.	8.5	Gingiva and cheek	Epidermoid cancer, Grade 1	No glands	14-0.6 mg. needles	3600 mg-br. pack 600 r x-ray	Well 6 yr.
xvt. Mrs. J.W.	2.0	Cheek	Adenocarcinoma, mucous type	No glands	7-0.6 mg. needles	3600 mg-hr. pack 600 t x-ray	Well 5 yr. 8 mo.
xvii. Mrs. R.L.S.	3.5	Gingiva and cheek with perforation	Epidermoid cancer, Grade 2	Large submax. gland	6—0.6 mg. needles 9—1.33 mg. needles	600 r x-ray	Local healing, extension in neck
XVIII. Mr. L.L.R.	2.0	Cheek	Epidermoid cancer, Grade 2	No glands	8-0.6 mg. needles 2-1.33 mg. needles	3600 mg-hr. pack 600 r x-ray	Well at 6 mo., untraced since
xix. Mrs. D.W.O	2.0	Gingiva and cheek	Epidermoid cancer, Grade 3	Large cerv. glands	8-0.6 cheek 1-1.33 cheek 6-2.4 glands	3600 mg-br. pack	Improved for 4 mo., more cervical extension thereafter
xx. A.G.D.	0.0	Entire cheek	Epidermoid cancer, Grade 1	No glands	16—1.33 mg. needles	3000 mg-hr, pack 600 r x-ray	Complete healing, died 3 yr. later, cause

	XXI. H.E.M.	3.5	Gingiva and cheek	Epidermoid cancer, no grade	No glands	9-0.6 mg. needles	3000 mg-hr. pack	Complete healing, died 2 yr. later, cause
	XXII. Mrs. C.W.	3.5×4.5	3.5×4.5 Entire cheek	Epidermoid cancer, no grade	Large subment. gland	7-1.33 check 4-0.6 all all all all all all all all all al	600 t x-ray	Local healing, more cervical extension at 4 mo.
	ххии. Мrs. M.C.	5.0	Entire cheek	Epidermoid cancer, Grade 1	No glands	10-2.4 mg. needles 6-1.33 mg. needles	300 F × 3 x-ray	Complete healing, no recurrence, died of another disease 5 yr.
2	xxiv. J.C.S.	3.5×2.0	Cheek	Epidermoid cancer, Grade 1	No glands	6-1.33 mg. needles 6-0.6 mg. needles	300 r×5 x-ray to each side	Well 5 yr., some leukoplakia present
ŧ.	xxv. G.A.P.	2.5	Cheek	Epidermoid cancer, Grade 4	Large subment. gland	8-0.6 3-1.33 cheek 2-2.4 3-2.4 gland	300 r×6 x-ray to neck	Local healing, other cervical glands at 3 mo.
	XXVI. G.D.	0.0	Entire cheek	Epidermoid cancer, Grade 1	Submax, gland	10—1.33 mg. needles 11—2.4 mg. needles	350 r X6 x-ray to neck	Complete local healing, more cervical extension in 6 mo.
	ххүн. Ј.Ғ.Мс	3.5	Ant. pillar and cheek	Epidermoid cancer, Grade 2	No glands	7—0.6 mg. needles 7—1.33 mg. needles	350 r×6 x-ray to neck	Small slough resected at 8 mo., well 4 yr.
<u> </u>	ххиш, М.Е.Т.V.	3.5	Cheek	Epidermoid cancer, Grade 2	Large submax, gland	4-1.33 cheek 7-2.4 cheek 4-1.33 gland	350 t X5 x-ray to neck	Well 4 yr. 3 mo.
	XXIX. A.L.W.	3.5	Ant. pillar and cheek	Epidermoid cancer, Grade 2	Subment, gland and bone	7—0.6 4—1.33 cheek 3—2.4 3—2.4 gland	350 r ×5 x-ray to neck	Very little improvement at 3 mo., un- traced
	xxx. Mrs. W.H.M.	3.0	Cheek	Epidermoid cancer, Grade 2	? Glands	7-0.6 mg. needles 4-1.33 mg. needles	350 r X6 x-ray to neck	Well 2 yr. 10 mo.
· · ·	XXXI. Mfs. J.T.D.	.6 5	Cheek	Epidermoid cancer, Grade 1	No glands	1—2.4 mg. needles 5—1.33 mg. needles 6—€.6 mg. needles	350 rX6 x-ray to neck	Well 3 yr. 3 m9,
1936	хххи. Ј.А.Н.	5.5	('heek	Epiderfflöld cancer, Grade 2	No glands	3—0.6 mg. needles 5—1.33 mg. needles	350 r×6 x-ray to neck	Well 2 yr. 5 mo.
. ,	хххиг. С.W.	6.0	Cheek and lip	Epidermoid cancer, Grade 1	No glands	3-1.33 4-0.6 Ip	300 r×12 x-ray to cheek and lip	Well 2 yr. 8 mo,
· 1	XXXIV. S.P.	3.0	Ant. pillar, cheek and gingiva	Epidermoid cancer, Grade 2	No glands	8—r.33 mg. needles 6—o.6 mg. needles		Local healing, deep recurrence at 5 mo.
	xxxv. Miss D.P.	0.5	Cheek	Epidermoid cancer, Grade 1	No glands	6-r.33 mg. needles	350 r X 5 x-ray to neck	Well 2 yr. 9 mo.

This extra radiation was soon found unnecessary and was abandoned.

Although the local improvement was encouraging from the start, it soon became evident that most of the failures resulted from the improper care of cervical metastases. An attempt was made to augment single erythema doses of 2000 kv. roentgen rays with 2 or 3 erythema doses delivered with a small radium pack made by placing two heavily filtered 50 mg. radium capsules on a balsa wood block designed to hold

reparable skin damage. This combined method was adopted because Quimby and Pack<sup>8</sup> showed a good many years ago that the combined effect of heavily filtered roentgen-ray and radium doses on the skin is less than that of equal amounts of either roentgen rays or radium rays alone. The roentgen therapy was administered at 220 kv., with 20 ma., a filter of 2.0 mm. of copper and 1.0 mm. of aluminum, a target-skin distance of 50 cm. and areas measuring 10.0 cm. on a side. The dosage obtained is

TABLE II

CURED CASES OF CARCINOMA OF CHEEK

Patient	Age	Size cm.	Pathology	Glands	Tobacco	Free of Disease
1 D.S.C. 1x W.L.N. xiv M.A.F. xv W.A.Y.	46 54 52 57	2.9 3.5 4.5 2.5	Epidermoid cancer, Grade 2 Epidermoid cancer, Grade 2 Epidermoid cancer, Grade 1 Epidermoid cancer, Grade 1	None None None None	Smoked 20 yr. Chewed years Chewed 30 yr. Chewed years	9 yr. 6½ yr. 6 yr. 6 yr.
xvi Mrs. J.W. xxiii Mrs. M.C. xxiv J.C.S. xxvii J.F.Mc. xxviii <b>W</b> .T.F.V.	53 48	2.5 5 0 3.5 × 2.0 3.5	Adenocarcinoma Epidermoid cancer, Grade 1 Epidermoid cancer, Grade 1 Epidermoid cancer, Grade 2 Epidermoid cancer, Grade 2	None None None None Submax.	Poor plate Snuff dipper Chewed years Chewed 45 yr.	5 yr, 8 mo. 5 yr. 5 yr. 4 yr.
XXX W.H.M. XXXI Mrs. J.T.D. XXXII J.A.H. XXXIII Miss C.W. XXXV Miss D.P.	73 54 74 50 60	3.0 3.5 2.5 6.0	Epidermoid cancer, Grade 2 Epidermoid cancer, Grade 1 Epidermoid cancer, Grade 2 Epidermoid cancer, Grade 2 Epidermoid cancer, Grade 2	gland None None None None None	Chewed years Snuff dipper Denies snuff Smoked years Snuff dipper Snuff dipper	4 yr. 3 mo. 2 yr. 10 mo. 3 yr. 3 mo. 2 yr. 5 mo 2 yr. 8 mo. 2 yr. 9 mo.

them at a distance of 2.0 cm. from the skin. Even when this pack remained in place for thirty-six hours the dose 1.0 cm. below the skin obtained with the combined treatment amounted to less than 5.0 T.E.D. and the results were indifferent. In 1933 a few of the glands were implanted with needles, using a dosage similar to that applied to the local lesion but although improvement occurred it soon became evident that 7.0 T.E.D. would not control metastatic carcinoma in lymph nodes. Divided doses of deep roentgen rays were then added to the implanted areas in the neck until it was learned empirically that 2,100 r might be given while the needles were in place at the rate of 350 r per day without producing irillustrated in Figure 4. The threshold erythema doses accredited to the radium needles may be obtained from Figure 1 and since 525 r produces I T.E.D. at a depth of approximately 2.0 cm., 4.0 T.E.D. may be added to the radium dosage at each point. The resulting figures show that the glands and their surrounding lymphatics receive from 10 to 13 T.E.D. That such a plan is effective has been proved in a previous paper,9 and the only patient in this series with a cervical node remaining well for more than three years (Case xxvIII) was so treated. The entire procedure is illustrated in Figure 6. This patient had a large carcinoma extending entirely through the cheek, and several hard non-tender glands were

palpable in the submaxillary and submental regions. The needles were placed so as to irradiate the involved nodes as well as the lymphatics beyond them. A dose of 2,100 r was given to an area measuring 10.0 cm. on a side while the radium needles were in place. The epithelitis produced on the skin healed in rapidly and no evidence of carcinoma can be detected either in the mouth or neck at the end of seven months. So many patients have responded well to this form of treatment that it has been adopted as a routine procedure in our office for all cases with intraoral carcinoma even when no palpable nodes are present. In a busy clinic where economic factors must be considered a technique which can be finished in one week has much to commend it.

Although the neck was efficiently treated in only the more recent cases reported in Table I the results are encouraging. A list of the 14 traced patients in which we have every reason to believe that a cure was produced is given in Table II. Cases XVIII, XX and xx1 may also have been cured but they are omitted from Table II because they could not be properly followed up. Although half of these cured patients have not as yet been free of malignant disease for five years, several observers have stated that cancer of the cheek very rarely recurs when it remains well for three years and it seems fair to claim a salvage of 40 per cent in the series of 35 cases treated. Since some of these patients will probably die of other causes before the five year period has expired, our figure of 40 per cent represents approximately the same number of cures as the 30 per cent five year salvage reported by Martin and Pflueger.

#### SUMMARY

- 1. Careful dosage calculations show that 7 to 8 threshold erythema doses can be delivered uniformly to intraoral tumors by means of weak radium needles placed parallel to one another in and around the lesion for a period of seven days.
  - 2. This plan is easily applied in the cheek

and a relatively small amount of radium is needed.

- 3. The 10 to 13 T.E.D., which in our opinion is needed to permanently control metastatic cervical lymph nodes, can be safely given with a combination of weak radium needles and divided doses of deep roentgen rays in a period of seven days.
- 4. In a series of 35 unselected cases of carcinoma of the cheek (mucosal portion) treated with the above plan 40 per cent appear to be well for periods of two and a half to nine years.

# REFERENCES

- CADE, S. Radium Treatment of Cancer. William Wood & Co., New York, 1929.
- 2. Martin, C. L. Small radium needles versus radon implants. Am. J. Roentgenol. & Rad. Therapy, 1932, 27, 240-248.
- 3. Martin, C. L. Irradiation therapy of malignant tumors of oral cavity, eye, ear, nose and throat. Ann. Otol., Rhin. & Laryng., 1935, 44, 426-441.
- 4. QUIMBY, E. H. Physical factors in interstitial radium therapy. Am. J. ROENTGENOL. & RAD. THERAPY, 1935, 33, 306-316.
- 5. Martin, H. E., and Quimby, E. H. Calculations of tissue dosage in radiation therapy; preliminary report. Am. J. Roentgenol. & Rad. Therapy, 1930, 23, 173-196.
- 6. Martin, H. E., and Sharp, G. S. Use of gold filtered radon implants in treatment of intraoral cancer. Am. J. Roentgenol. & Rad. Therapy, 1931, 26, 28-38.
- 7. Martin, H. E., and Pflueger, O. H. Cancer of the cheek (buccal mucosa). *Arch. Surg.*, 1935, 30, 731-747.
- 8. Quimby, E. H., and Pack, G. T. Skin erythema for combinations of gamma and roentgen rays. *Radiology*, 1929, 13, 306-312.
- 9. Martin, C. L. Treatment of malignant cervical lymph nodes with irradiation. Am. J. Roentgenol & Rad. Therapy, 1939, 41, 819-831.

# DISCUSSION

Dr. Harold G. F. Edwards, Shreveport, La. I have enjoyed Dr. Martin's paper very much. It brings out one point and that is that with radium therapy there are many techniques, like the railroads, there are many running into St. Louis and all of them have brought you here safely. I think all of us probably have a little different type of technique.

I have been using platinum needles since

early 1932 and my set-up is a little different from that of Dr. Martin. My 27 mm. needles are I mg. of radium with filtration of 0.5 mm. platinum and an active length of 16 mm. While the 2 mg. needles are 44 mm. im length, the 3 mg. are 60 mm. and I have some 4 mg. which are 76 mm. More recently, because of the mail limitations on radon shipments, I have purchased the small platinum element implants devised by Dr. Pack.

The needles which I make use of as a rule are left in the epidermoid types of carcinoma for eight days. In a lip, making use of seven I mg. platinum needles, if the tumor isn't too extensive, they are left in eight days. If, on the other hand, the tumor is bulky, additional needles of 2 mg. are put in at the peripheral zones. Treated in this manner, we have not failed to secure primary healing and the patient has remained cured, many of them over a five year period.

I have found that the small Pack implant will work well in carcinoma at the base of the tongue when implanted, by a simple incision through the skin, just above the hyoid bone, under bloc infiltration; implantation is done through the trocar into the base of the tongue.

In using platinum needles in the oral cavity, I have not made use of sutures but rather have attempted to place the needles in such a fashion that they interlock and when so placed, we cross-tie them. I think that this causes less trauma and may solve the one problem which, in my opinion, is the one great cause of necrosis following interstitial irradiation: infection. I think that a great many of these sloughs we see following interstitial irradiation and heavy roentgen irradiation unquestionably come about because of secondary infection.

With regard to the metastatic nodes in the neck, first of all we must prove that the mode is carcinomatous. It is quite true that in a patient who has had a proved epidermoid carcinoma of the oral cavity and later develops an enlarged node it is usually malignant, but the procedure to prove it is such a simple one that we should not treat the patient until this is done. Furthermore, it offers us additional information as to whether or not this node has undergone some liquefaction and has starzed to break down. If it has, it presents quite a different problem.

I believe that by simple aspiration of a metastatic node and placing the material on a slide and crushing it and holding it up to the light, by just macroscopic evidence we are able to say in about 85 to 90 per cent that this is metastatic carcinoma. It presents a mealy appearance on the slide, somewhat as the old Bass-Watkins typhoid agglutination test did. Further study can be made immediately by staining with hematoxylin and eosin, finding the epithelial scales and in some instances the metastatic cells with many mitotic figures.

If the node is small and we feel sure it has not perforated the capsule, then I prefer to cut down on the node, using local anesthesia, and use the small Pack radium element implants. Previously I had been using radon. I believe that this is preferable to intensive roentgen therapy first and then needles immediately following; because we are treating only one small node and then we have preserved the skin and underlying structures so that if a subsequent node does develop, we can again attack it in the same manner and still preserve the structures in the neck, while if we have irradiated heavily, using rather large roentgen fields and follow with interstitial irradiation, we have almost closed the door to any future therapy.

When the node has perforated the capsule, which we feel is evidenced by fixation and liquefaction in the node, then I employ a method similar to Dr. Martin's: giving a daily fraction of 200 r, running up to approximately 3,500 r, and immediately under general anesthesia place the large needles, the 4 mg., which are 76 mm. in length, without regard to blood vessels, nerves or whatnot, deeply into the tissues and into the node where possible. These are left in eight to ten days and we may use as high as 50 mg. in this fashion if the distribution is wide enough. With regard to distribution, of course it is ideal to think of distribution with the idea of spheres, but this is almost impossible to achieve. I think Mrs. Quimby's tables have certainly given us a guide by which we should travel and without which we would probably have gotten into much trouble.

As for myself, I feel that it is much better to overdose rather than underdose because if you underdose you cannot go back and treat your patient again, whereas if you overdose, if there is some slough and the distribution has been wide enough, you will get rid of all carcinoma cells in most instances and your patient will be cured of his cancer, while underdosage will sooner or later mean a dead patient.

# THE RELATION OF MEAL TEMPERATURE TO GASTRIC MOTILITY AND SECRETION\*

By J. GERSHON-COHEN, M.D., HARRY SHAY, M.D., and S. S. FELS PHILADELPHIA, PENNSYLJANIA

THE gastric temperature was obtained with a series of three iron-constantan thermocouples passed into the stomach with the leads conducted to the potentiometer through one side of a partitioned or double-barrelled Miller-Abbott tube. The thermocouples were coated with bakelite varnish to protect them from the action of the hydrochloric acid in the stomach. The precision of this thermometer was within 0.2° F. as checked against a standard precision mercury thermometer.† The temperature was then continuously recorded on graph paper. The subjects were obtained from among patients in our practice who were found to be healthy after careful examination; and this included elimination of all those emotionally unstable or neurotic as well as those with organic disease. A fractional gastric analysis was done simultaneously with the recording of temperature so that its bearing on gastric motility might not be overlooked. The test meal for all motor and secretory studies was 3 ounces of barium sulphate dissolved in 250 cc. of 2 per cent Liebig's extract. Extractions of 10 cc. of stomach contents were made every fifteen minutes through the other barrel of the partitioned Miller-Abbott tube during the period of temperature recording and each experiment was terminated when the stomach was emptied, determined by the extraction method and by roentgenoscopic observation. Some subjects were studied in the morning after a fifteen hour fast and others were studied in the evening after a nine hour fast.

The first test was made with a meal at body temperature varying from 98–99° F. The findings were checked two or three

times and the subject used for further study only if the results were consistent; in this way, we hoped to eliminate those in whom the presence of neuropsychic factors might have presented indeterminable variations.

At the next test, done usually after an interval of one week—after determining complete evacuation of the previous barium-Liebig meal—the temperature of the meal varied from 35-40° F. The third examination was made with a meal heated to 140-145° F. A few determinations were made with the meal at room temperature.

The secretory studies of the stomach comprised determination of free and combined hydrochloric acid by titration; total chlorides by the method of Wilson and Ball and the quantitative determination of pepsin by a slight modification of the Polland and Bloomfield method.

# COMMENTS

In the 24 subjects used for these experiments, the gastric temperature varied from individual to individual much like the mouth and rectal temperature, extending from 97.4 to 99.6° F. The stomach temperature of each subject was noted continuously for fifteen minutes or more before ingestion of the various test meals. With the meal of 35° F., a marked immediate drop in gastric temperature occurred after ingestion, usually to 70-75° F. This drop in temperature strikingly demonstrates the capacity of the mouth, pharynx and esophagus to rapidly heat an ice-cold drink. While this rapid initial heating changes the gastric temperature from 35 to 70° F. the contents do not reach body temperature for thirty to forty minutes.

A hot drink taken at 145° F., which is as high as the average subject can tolerate,

<sup>†</sup> The thermocouples were made for us by Dr. A. N. Lucian, of the Research Physics Department, University of Pennsylvania.

<sup>\*</sup> Read at the Thirty-Ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J.; Sept. 20-23, 1938.

is cooled almost immediately on entering the stomach to 106–110° F. and reaches body temperature within fifteen to twenty minutes.

The differences in gastric motor reactions to meals of widely different temperatures seem interesting. The cold meal begins to leave the stomach almost immediately and rushes more rapidly than usual through the jejunum and ileum. The increased motility is most marked soon after ingestion corresponding to the period

with the hot meal. With the cold meal, there is an actual depression of gastric secretions at first when the temperature is most markedly lowered; but within a shorter time than it takes for the gastric temperature to return to normal, gastric secretion is normally resumed. The curves in Figure 3 were plotted with correction of the dilution factors. They show the effect on the secretion of hydrochloric acid by test meals of different temperatures. Since more than normal gastric evacuation of

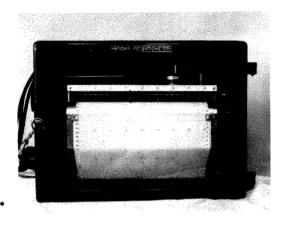




Fig. 1

of greatest depression of gastric temperature; and as the gastric temperature returns slowly to normal, there develops a progressive slowing in gastric evacuation so that by the time the temperature of the gastric contents reaches normal (in thirty to forty minutes) motility is normal.

The hot meal, on the other hand, is slower to leave the stomach at first, but soon empties normally or even slightly faster than normal. Since it is usually difficult to drink liquids heated higher than 40-50° F. above body temperature, it seems to take the stomach less time to bring this meal to body temperature than it does the cold meal imbibed at 65° F below body temperature. It is probably for this reason that the intestinal patterns of the hot meal are not so markedly altered as by the cold meal.

No appreciable abnormal deviations were noted in the gastric secretory changes

the cold meal takes place soon after ingestion, the intestines are filled with more than the average amount of contents inadequately acted upon by the gastric juices. This might be one of the factors responsible for some of the diarrheas during the summer when the American custom of taking excessive ice-cold drinks is so generally followed.

## DISCUSSION

John Hunter<sup>1</sup> in 1778 recorded stomach temperatures in cold-blooded animals and in 1878, Kronecker and Meyer reported experiments, using small maximum thermometers, which they permitted dogs and rabbits to swallow. When the thermometers were expelled from the rectum, the maximum temperature in the intestinal canal could be read. In order to determine the stomach temperature, they pulled the thermometer from the stomach by means of a

# GASTRIC MOTILITY AND INTESTINAL PATTERNS AFTER HOT AND COLD MEALS

Normal 78°F.	Cold 360-380F.	Hot 135°-145°F	(An adult male with normal gastric secretion)
	The state of the s	.9	5 minutes  There was greater initial motility of the cold barium-liebig extract meal than of the same meal at room temperature while the hot meal progressed no farther than the duodenal cap during the first 5 minutes.
			During this period, the cold meal continued to empty faster and the hot meal slower than the meal at room temperature.
			30 minutes During this interval, emptying continued as during the preceding 15 minute period, but with progressively less difference in the rate. At this time, the cold meal residue in the stomach had reached the normal body temperature.
			During the past 15 mimute interval, all three meals seemed to empty from the stomach at the same rate.
Temperature Fahrenheit 115 110 105 100 95 90 85 80 75		Temperature ourvingestion tempera	ture 152°F.

Fig. 2

thread. The temperature of the stomach was found to be 0.9° F. lower than the rectum. Beaumont (1825–1833) was the first to determine stomach temperature in man in his famous subject with the gunshot gastric fistula. The temperature in this case averaged 100.2° F. and varied from 98.1 to 100.8° F. Later Quincke (1889) determined the gastric temperature with a

thermometer in a boy with a gastrotomy. In this instance, the gastric temperature was 0.27° F. higher than in the rectum. A similar experiment was carried out by Ranckin and Tigerstedt (1908) in a boy with a gastric fistula. They found the gastric temperature to be 0.36° F. above the rectal temperature. Winternitz (1881) seems to have been the first to measure

gastric temperature in normal subjects. He fastened a 4 cm. maximum thermometer to the tip of a rubber tube which was passed into the stomach. The experiments were designed only to ascertain the effects of external body chilling, and no numerical record of the gastric temperature is given. In 1917, Stengel and Hopkins seem to have been the first to record stomach temperatures with a thermocouple with a gal-

supply a numerical record of gastric temperatures. Foged used a similar procedure, but extended the studies to include large numbers of normal subjects so that his findings are probably the most authentic. In Philadelphia, Hepburn, Eberhard, Ricketts and Rieger did some splendid work with gastric temperature recordings and made some determinations of associated gastric secretory changes. No roentgeno-

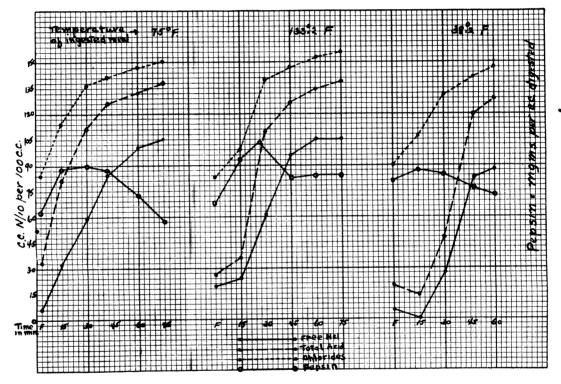


Fig. 3

vanometer and a potentiometer, the readings being taken in microvolts. The wires were run through an Einhorn tube. In 1925, Reis described a method for graphic registration of gastrointest nal temperature. He used an electrical resistance thermometer. The conductors were enclosed in an opaque tube, and its position in the intestinal tract could so be seen easily by use of the roentgenoscope. In Reis's work, there is no numerical record of gastric temperature. Kotschau and Roeloff (1927) used a thermocouple at the tip of a duodenal tube and were probably the first to

logic records of gastric or intestinal motility were made. Our gastric temperature recordings agree essentially with the findings of these previous investigators. None of them, however, had carried out simultaneous determinations of gastric motor and secretory activity. While we have found some effect on gastric motility by hot and cold meals which resulted in varying roentgenologic intestinal patterns, we did not find an appreciable effect on gastric secretion, except for a short period following the ingestion of an ice-cold meal.

#### SUMMARY

- 1. The normal gastric temperature as determined with sensitive thermocouples is approximately 99° F. and seldom varies more or less than 1° F. Its variation from subject to subject is as great as the mouth temperature.
  - 2. An ice-cold liquid test meal chills the stomach 25-30° F. and it takes thirty-five to forty-five minutes before the gastric contents return to normal gastric temperature.
  - 3. A hot liquid meal at 145-155° F. raises the gastric temperature immediately 6-10° F. which is overcome in fifteen to twenty minutes.
- 4. The colder the meal, the greater seems the rate of gastric evacuation.
- 5. Hot meals may empty more slowly than cold meals immediately after ingestion, but soon compensate by increased emptying after a short interval.
- 6. No appreciable effect has been noted on gastric secretion by very hot meals, but cold meals depress gastric secretion during the initial stages of digestion.
- 7. Summer diarrhea might be due partly to ice-cold drinks which effect too rapid gastric evacuation of gastric contents not effectively prepared for the intestines because of the depression in gastric secretions.

# REFERENCES

1. Foged, J. Temperature in stomach, esophagus and pharynx under normal conditions. *Ugeskr*. f. laeger., 1933, 95, 163–169.

2. Hepburn, J. S., Eberhard, H. M., Ricketts, R., and Rieger, C. L. W. Temperature of the gastro-intestinal tract; effect thereon of hot and cold foods and of physical therapeutic agents. *Arch. Int. Med.*, 1933, 52, 603-615.

3. Stengel, A., and Hopkins, A. H., A new method for determining the intragastric temperature in man, with some observations of its variations after ingestion of hot and cold liquids and during digestion. Am. J. M. Sc., 1917, 153, 101-106.

## DISCUSSION

Dr. T. Grier Miller, Philadelphia. A few days ago, before seeing Dr. Gershon-Cohen's paper and knowing little about the subject, I asked one of my associates, Dr. Hugh Mont-

gomery, if he would not do for me an experiment on gastric temperature in man. He induced Dr. Abbott, of our staff and who is an expert at such things, to swallow a thermocouple and then eat some ice cream and drink a bottle of cold Coca-Cola. That produced a fall of Dr. Abbott's gastric temperature to 15° C. and it was thirty minutes before it reached normal again. Then he took a drink of hot water (50° C.), whereupon the temperature rose to 46° C. and dropped back to normal only after about twenty minutes.

These results, though surprising to me at the time, are in agreement with those of Dr. Gershon-Cohen and his associates. They are also in entire agreement with the data obtained by Stengel and Hopkins in our clinic more than twenty years ago. Stengel and Hopkins also studied the variation in temperature between the fundus and pylorus after hot and cold drinks, finding that it was always less affected in the pylorus.

Dr. Gershon-Cohen states that simultaneous investigations of the secretory and motor phenomena after hot and cold meals had not previously been made, which I believe to be correct, and he makes no reference to any earlier roentgen investigations of motility. I think, however, that mention should be made of the supplementary work of Weitz and Sterkel (1920) who observed a change from the "fishhook" to the "steer-horn" type of stomach in subjects exposed to a cold environment; also to that of Sleeth and Van Liere (1937) who by the use of a barium meal found that external cold shortened the emptying time and external heat increased it. Kuenzel and Todd (1929), on the contrary, observed, under the fluoroscope. that external heat increased the activity and contraction of the stomach; also, that hot drinks had a similar effect.

In contrast to these observations Muller (1905), by administering fluids at varying temperatures and evacuating the stomach fifteen minutes later, concluded that the motility was greatest when the fluid approached body temperature. Basch and Mautner more recently (1930) found that greatest diuresis followed the intake of fluids of normal temperature. Their work, perhaps, in view of the present report, deserves repetition.

As to secretory changes, no reports after the ingestion of substances of varying temperatures have been found, but Yamana reported last year that ice packs applied to the abdominal

wall of rabbits and of man caused an increase in the quantity and acidity of the gastric contents, and Bogendorfer and Sell (1930) found a similar rise in secretory activity after cold applications but a diminution after heat. Fischer (1920), also, working with dogs having a Pavlov pouch, found that hot air baths reduced the quantity of secretion by 50 per cent.

Thus this literature, though not entirely consistent, suggests that cold increases the motor and secretory activity of the stomach, while heat has the opposite effect. The present work confirms that opinion as to the motor effects of cold substances in the stomach but otherwise indicates no striking changes after either cold or hot meals. I believe that the work reported here has been well done and that the results, tentatively at least, should be accepted.

Dr. John L. Kantor, New York City. This work is clinically very helpful. It extends the previous observations which are a little paradoxical and somewhat confusing, and helps us understand the situation better.

As far as heat and cold are concerned, they work in the opposite direction according to whether the temperature is applied externally to the skin, or internally within the gut. Once that is understood, I think the rest is simple. In other words, as I understand t, it has here-tofore been shown that heat applied externally to the skin relaxes spasm and depresses tone; heat applied internally within the lumen increases the tone of the viscus. Cold acts the opposite in both cases.

What has not hitherto been shown and therefore is the crux of this afternoon's presentation, is the behavior of the pyloric sphincter.

The question in my mind up to this very afternoon was, if heat applied internally increases tone, what happens to the sphincter? From what we have heard today, heat internally increases tone and at the same time seals the sphincter temporarily. This, however, is to be regarded as a benefit because of the im-

proved gastric secretion and the increased time available for gastric digestion.

All this is in keeping with our clinical impression as to the harmfulness of cold drinks, which not only pass through quickly, carrying the cold into the bowels, but result in impaired juice content. The benefit of hot drinks is due to the opposite effect.

Finally, if one may bring this down to clinical usefulness, it would seem that we probably over-cold-feed some patients. The whole Sippy regimen is commonly administered on the ice-cold basis, and in my practice, the postoperative stomach at least is never treated on an ice-cold basis. I think heat is the thing that is needed, and I would therefore suggest that it may be also useful to heat some, if not all, the diets in the ulcer regimen.

DR. GERSHON-COHEN (closing). I should like to thank Dr. Miller and Dr. Kantor for their cordial résumé of this subject. We are particularly indebted to Dr. Miller for the fine tube that we now have at our disposal, which has opened up a tremendous new field of study in small intestinal conditions.

In the presentation of our paper, we studiously avoided mentioning anything about the effect of external chilling or external heating because that is a big problem on which there is already an extensive literature. The literature is scanty, however, in the field where the temperature of the meal itself has been studied.

We are carrying out a series of experiments with external heat and chilling in which the patients have showers before we give them their test meal, hot showers and cold showers, and immersion in water at different temperatures.

Essentially, all these experiments demonstrate the points that Dr. Kantor made and the probabilities are that when comparison is made between external and internal changes of temperature, the findings will be very much as Dr. Kantor very well outlined here this afternoon



# VITAMIN B: IN IRRADIATION SICKNESS

## PRELIMINARY REPORT

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NTENSIVE roentgen and radium therapy in the treatment of cancer and allied diseases is occasionally complicated by the development of dizziness, anorexia, nausea, and vomiting. If the symptoms are not marked, interruption of radiation therapy is not indicated, but persistent nausea and vomiting necessitate discontinuance of the treatment unless these symptoms can be controlled by some form of medication. This paper deals only with those cases which exhibited severe symptoms of irradiation sickness and then received oral or parenteral synthetic vitamin B<sub>1</sub> (thiamin chloride)\* therapy. A total of 21 cases, summarized in tabular form, is presented in this report. In 7 of these cases, irradiation was directed to the breast area, 4 patients being treated by interstitial radium element needles. Of the remaining 14 cases, 12 received irradiation to the pelvis, I to the liver and spleen, and I to the left side of the neck.

A factor to be considered is the relative efficacy of the oral and parenteral preparations of vitamin B<sub>1</sub>. In comparing the two methods of administration, the quantity of the drug used and the length of time necessary to produce complete relief of symptoms are important considerations. Marked anorexia, nausea, and dizziness can usually be controlled by 3,000 international units (I.U.) daily of the oral preparation, but where nausea, anorexia, and vomiting are present it is necessary to increase the dosage of the oral preparation to 6,000 I.U. or more daily for alleviation of the symptoms. In the majority of cases where the oral preparation of the drug is used, definite

improvement does not occur before twentyfour to forty-eight hours. In contrast to
this, the njected vitamin B<sub>1</sub> gives appreciable or complete relief within one to
three hours. Cases x1 and x11 in Table 1
required 6 000 1.0. of the oral preparation
daily to control the ill effects of irradiation.
In order to note the relative amount required, the medication in both these cases
was changed to the hypodermic form,
using one-half the oral dose, and complete
freedom from symptoms was maintained
with the daily use of 3,000 1.0. of the hypodermic preparation.

Sponheimer<sup>3</sup> reports only slight improvement in symptoms as a result of oral administration of vitamin B<sub>1</sub>, but states that complete relief was obtained by the use of the parenteral therapy. Martin and Moursund<sup>2</sup> report favorable results following administration of the oral preparation, and they resort to intramuscular injection only when vomiting occurs. These authors have observed that where serious complications, such as par ial bowel obstruction, are present, vitamia B1 therapy is ineffective. We have obserzed one such case, Case x in Table 1, which did not show definite response to v tamin B<sub>1</sub> therapy. Autopsy in this case disclosed the presence of a partial bowel obstruction in the region of the cecum.

We find that daily injections of 3,000 i.u. will, in the majority of cases, give rapid and complete relief. Infrequently, a recurrence of symptoms requires a temporary or permanent increase in the dosage. One patient receiving roentgen therapy to the left side of the neck required a temporary increase to 4,500 i.u. daily by hypodermic injection for control of recurrent nausea. In only a small percentage of cases

<sup>\*</sup> Synthetic vitamin  $B_{\rm I}$  (thiamin chloride) used to carry out this clinical survey was supplied as Betaxin by courtesy of the Medical Research Department of the Winthrop Chemical Company, and as Betalin S by courtesy of Eli Lilly and Company.

TABLE 1
SUMMARY OF 21 CASES OF IRRADIATION SICKNESS RECEIVING VITAMIN B<sub>1</sub> THERAPY

Diagnosis			Roentgen Therapy	Radium Therapy	Other Therapy None	Symptoms Anorexia, nausea, and	Dosage of Vitamin B <sub>1</sub>	Results Rapid control of all symp-
Carcinoma simplex, None		None		Interstitual radium element needles to breast; 102 mg. ra- dium for 19,227 mg- hr.	None	Anoteway, and vomiting after 3,000 mg-hr. of irradiation. Recurrence of nausea 24 hours after stopping the medication	Injection of 3,500 f.c. vary for 8 days. Medication stopped on day of removal of radium. Injection of 3,000 f.c. daily for 3 days for recurrent nausea.	toms during periods of Bi administration
Carcinoma simplex, None left breast		None	And a second section of the second section sec	Interstitial radium element nerdles to breast; 103 mg. radium for 26,471 mg. hr.	None	Anorexia, nausea, and vomiting after 4,000 mg-hr. of irradiation. Recurrence of nausea 40 hours after stopping the medication	Injection of 3,000 Le, daily for 7 days. Medication supped after 1,000 mg hr. Injection of 1,500 Le, daily for 2 days, then 450 Le, orally for 5 days	Rapid control of all symptoms during periods of B <sub>1</sub> administration
Carcinoma simplex, None left breast	Management & Real Park Specimens (1) and the Specimens (2) and the Specimens (3) and the	None	A CONTRACTOR OF THE CONTRACTOR	Interstitial radium element needles to breast; 109 mg. radium for 23,896 mg-hr.	None	Anorexia, nausea, and vomiting after 4,000 mg-hr. of irradiation	Injection of 3,000 1.0. daily for 2 days. Dosage increased to 6,000 1.0. daily for 3 days. Dosage increased to 10,000 1.0. daily for 4 days	Definite improvement with dosage of 3,000 and 6,000 LU. daily. Absence of all symptoms with 10,000 LU. daily
Carcinoma simplex, One port right breast left breast, postop- and each axilla for earlive. Carcinoma 1,600 r to each port. Simplex, right breast for 650 r to each port for 650 r to each port.		One port right hand each axilla 1,600 r to each Iwo ports pitt or 650 r to each	tht breast axilla for each port. pituitary each port	None	None	Anorexia, nausea, and dizziness 15 days after institution of therapy	Injection of 3,000 1.v. daily for 2 days. Dosage increased to 6,000 1.v. daily for 3 days	Complete relief with daily dosage of 6,000 LV.
Carcinoma simplex, Cases Iv and v are same left breast, postop-patient. See therapy above. Radium thersimplex, right breast apy 13 days after completion of roentgen therapy		Cases Iv and v arespatient. See the above. Radium 1 apy 13 days after oletion of roen therapy	are same therapy m ther- ter com- roentgen	Interstitial radium element needles to right breast; 95 mg. radium for 16,072.5 mg-hr.	None	Nausea and vomiting after 2,400 mg-hr. of irradiation. Reduced dosage of B <sub>1</sub> followed by recurrence of nausea	Injection of 6,000 1.v. daily for 2 days. Dosage reduced to 3,000 1.v. daily for 3 days. Dosage increased to 6,000 1.v. daily for 3 days	Daily dose of 6,000 1.v. necessary for complete relief of symptoms
Carcinoma simplex, Three ports right bright breast for 2,000 t to each	Three ports ri for 2,000 r to	Three ports right b	ght breast each port	None	None	Anorexia, nausea, and dizziness 15 days after institution of therapy	Injection of 3,000 i.v. daily for 6 days. Dosage increased to 6,000 i.v. daily for 11 days	Symptoms alleviated with 3,000 1.0. daily. Absence of all symptoms with 6,000 1.0. daily
Inflammatory carci- Two ports left breast for 1,850 r to each port.  One port left supraclavicular region and one port left axilla for 1,775 r to each port	Two ports for 1,850 r to One port le clavicular r one port left 1,775 r to ea	Two ports left b for 1,850 r to each One port left su lavicular region one port left axill 1,775 r to each po	each port. It supra- gion and axilla for ch port	None	None	Anorexia, nausea, and vomiting 24 days after institution of therapy	In jection of 3,000 1.v. daily for 8 days	Rapid control of all symptoms

symptoms during periods of B <sub>1</sub> administration	Rapid control of all symptoms. Recurrent nausea treated satisfactorily with temporary increase in dosage. Uncontrollable nausea with previous roentgen therapy to pelvis	Some relief of nausea during periods of B, administration. Invasion of cecum with partial bowel obstruction revealed at autopsy	6,000 L.U. orally necessary to control symptoms. Complete relief with daily injection of 3,000 L.U.	6,000 1.0. orally necessary to control symptoms. Complete relief with in- jection of 3,000 1.0. daily	1,500 I.U. daily did not give complete relief. All symptoms controlled by daily injection of 3,000 I.U.	Rapid control of all symptoms
for 13 days, 450 i.u. orally for 12 days between the two series of roentgen treatments. Injection of 3,000 i.u. daily for 18 days	Injection of 3,000 1.0. daily for 8 days. Injection of 4,500 1.0. daily for 5 days. Injection of 3,000 1.0. daily for 12 days	Injections of 1,500 1.0. daily for 7 days, then stopped for 2 days. Daily injection of 1,500 1.0. resumed and given for 13 days	3,000 i.e. orally for 2 days; 6,000 i.e. orally for 2 days. Injection of 3,000 i.e. daily for 16 days	3,000 L.U. orally for 2 days; 4,500 L.U. orally for 1 day; 6,000 L.U. orally for 4 days. Injection of 6,000 L.U. daily for 2 days. Injection of 3,000 L.U. daily for 14 days	Injection of 1,500 t.v. daily for 5 days. Injection of 3,000 t.u. daily for 20 days	Injection of 3,000 1.0. daily for 20 days
weakness 2 days after institution of therapy. Recurrence of nausea with second series of roentgen treatments	Anorexia and nausea 4 days after institution of therapy. Recurrence of nausea 13 days after institution of therapy	Persistent nausea and anorexia and occasional voniting prior to roentgen therapy. Roentgen therapy aggravated all symptoms	Anorexia, nausea, and vomiting 16 days after institution of roentgen therapy. Radium therapy produced no symptoms	Extreme anorexia and nausea 3 days after institution of roentgen therapy	Anorexia, nausea, and dizziness 3 days after institution of roentgen therapy. Radium therapy produced no symptoms	Anorexia and nausea 3 days after institution of roentgen therapy.  Radium therapy produced no symptoms
A FAINSTUSTORIS	None	Intravenous glucose, Liver extract, Trans- fusions	None	None	None	None •
None	None	None	Intrauterine and intravaginal radium for 9,216.9 mg-hr. Radium therapy started 3 days after completion of roentgen treatments	None	Intrauterine and intravaginal radium for 9,350-4 mg-hr. Radium therapy started to days after completion of roentgen treatments	Intrauterine and intravaginal radium for 7,702.4 mg·hr. Radium therapy started I day after completion of roentgen treatments
Directly to liver and obliquely to spleen for 8,000 r to each port. Both superalexicular areas, left axilla and right groin for 330 r to each of four ports	One port to left neck for 2,000 r. Two ports pituitary for 650 r to each port	Three anterior and three posterior ports to pelvis for 160 r to each port, 19 days later same ports used for 320 r to anterior and 240 r to posterior ports	Three anterior and three posterior ports to pelvis for 2,150 r to each port	Three anterior and three posterior ports to pelvis for 1,600 r to each port	Three anterior and three posterior ports to pelvis for 2,000 r to each port	Three anterior and three posterior ports to pelvis for 2,200 r to each port
Hodgkin's disease	Basal cell carcinoma of cervix. Epider- moid carcinoma in subcutaneous tissues of neck	Carcinoma of cervix	Papillary squamous carcinoma of cervix	Squamous carcinoma of cervix	Squamous carcinoma of cervix	Anaplastic epider- moid carcinoma of cervix
50 E	<del>2,</del> 1.4.	\$\psi\$	Se	124	<b>7</b> 4	धुर
VIII	×	×	IX	×	X	XIX

Table I—(Continued)

	itamin B <sub>1</sub> Results	co 1.U. daily Rapid control of all symptoms	oo i.u. daily  Complete control of all threurrence symptoms during periods injection of B, administration for 9 days	© 1.U. daily injection of 6,000 t.u. nection of 6,000 essary for effective condays. Injection of all symptoms 7.1 day, fn-1.u. daily for	00 I.V. daily Rapid control of all symptoms	for 5 days Complete control of all symptoms within 36 hours	for 2 days; 6,000 I.U. orally necessary for 13 days to control symptoms	Alleviation of symptoms, for 3 doses but not so satisfactory as when medication given daily. Uncontrollable nausea with previous roenigen therapy to right breast
	Dosage of Vitamin B <sub>1</sub>	Injection of 3,000 1.U. daily for 10 days	Injection of 3,000 1.v. daily for 10 days. With recurrence of symptoms, injection of 3,000 1.v. daily for 9 days	Injection of 3,000 1.0. daily for 2 days. Injection of 6,000 1.0. daily for 5 days. Injection of 3,000 1.0. I day. Injection of 6,000 1.0. daily for 4 days	Injection of 3,000 I.u. daily for 3 days	3,000 1.0. orally for 5 days	3,000 1.U. orally for 2 days; 6,000 1.U. orally for 13 days	Injection of 6,000 LU. on alternate days for 3 doses
	Symptoms	Nausea, dizziness, and vomiting 12 days after institution of roentgen therapy	Nausea and vomiting 2 days after institution of roentgen therapy. Recurrence of symptoms 30 hours after stopping medication	Nausea and vomiting 18 days after institution of roentgen therapy. Recurrence of symptoms with reduced dosage of B <sub>1</sub>	Anorexia, nausea, and dizziness 22 days after institution of roentgen therapy	Roentgen therapy produced no symptoms. Anorexia and nausea after \$,000 mg-hr. of irradiation	Anorexia, nausea, and dizziness on day of first roentgen treatment	Anorexia and nausea 7 days after institution of roentgen therapy
	Other Therapy	None	None	Transfusions	None	None	None	None
	Radium Therapy	None	None	Intravaginal radium for 2,160 mg-hr. to control bleeding	None	Intrauterine and intravaginal radium for 9,986.6 mg-hr.	None	None
ACT TO THE RESIDENCE OF THE PROPERTY OF THE PR	Roentgen Therapy	Two anterior and two posterior ports to pelvis for 1,600 r to each port	Three anterior ports to pelvis for 2,000 r to each port	Three anterior and three posterior ports to pelvis for 2,200 r to each port	Three anterior ports to pelvis for 3,400 r to each port, and three posterior ports to pelvis for 3,200 r to each port	Three anterior and three posterior ports to pelvis for 3,200 r to each port	Ovarian castration with two anterior and two posterior ports for 960 r to each port	Ovarian castration with two anterior ports for 960 r to each port. Two ports to pituitary for 650 r to each port
	Diagnosis	Squamous carcinoma of cervix	Squamous carcinoma of cervix	Anaplastic carcinoma of cervix	Multiple papillomata of bladder	Anaplastic carcinoma of cervix	Inflammatory carcinoma, right breast	Carcinoma simplex, right breast
The Profession of the second	Age and Sex	277	61 F	39 FF	4=	e e e e e e e e e e e e e e e e e e e	74	F36
Memorrowania	Case	ΛX	IAX	IOX	хуш	XIX	XX	XX

is it necessary to increase the daily injections to 6,000 1.U. or more. One patient, treated by application of interstitial radium element needles to the left breast area, required daily injections of 10,000 1.U. to eliminate nausea and vomiting. The results obtained with the hypodermic preparation are definitely superior to those following use of the oral preparation. We have therefore discontinued the oral therapy except for purposes of study.

The treatment of out-patients presents a different problem in that those patients who develop irradiation sickness cannot be satisfactorily relieved of their symptoms simply by the oral administration of large doses of vitamin B<sub>1</sub>. Many such cases feel so ill that it is difficult to retain their confidence and cooperation, with the result that they fail to continue the medication as prescribed and occasionally refuse to follow the course of radiation therapy as outlined. This undesirable factor can be overcome by requiring the patient to return to the hospital or to his physician for daily injections of vitamin B<sub>1</sub>. Sometimes it is necessary to hospitalize these patients in order to secure their cooperation and treat them effectively. We have treated outpatients receiving irradiation three times each week by giving them an injection of vitamin B<sub>1</sub> on the days when they received roentgen therapy. This particular usage of the drug did not prove effective, and symptoms were not completely controlled unless the patient was given daily doses of vitamin B<sub>1</sub>. It is therefore apparent that smaller daily doses are more effective in the control of irradiation sickness than are massive doses given on alternate days.

A number of in-patients who developed irradiation sickness were effectively relieved by vitamin  $B_1$  therapy, which was then temporarily discontinued in order to note recurrence of symptoms and the time factor in their reappearance. In all such cases there was a return of the nausea and anorexia within twenty-four to forty-eight hours after the medication was stopped. This finding further emphasizes the value

of the daily administration of vitamin B<sub>1</sub> in preference to larger doses of the drug given every other day.

Martin and Moursund<sup>2</sup> have called attention to the fact that serious symptoms are produced only when some portion of the intestinal tract or the parotid gland is included in the area under treatment. Our findings differ somewhat in that we have not found that radiation therapy to the parotid region is apt to produce severe symptoms. We have, on the contrary, observed less incidence of irradiation sickness in cases where therapy was directed to the parotid region than in those receiving radiation therapy to other portions of the body. A number of cases of irradiation sickness have been observed among patients receiving massive deses of radiation in the form of interstitial radium element needles for cancer of the breast. Four of the cases treated by interstitial radium element needles are summarized in Table 1.

We have had one patient, Case XIX in Table I, symptomless during roentgen therapy to the pelvis, who developed marked anorexia and nausea following intrauterine and intravaginal application of radium. This case demonstrates irradiation sickness following protracted irradiation, and the symptoms were here effectively controlled with 3,000 I.U. daily of the oral preparation. Of all the cases which suffered ill effects from intensive roentgen therapy to the pelvis, none has shown a recurrence of symptoms during the following intrauterine and intravaginal application of radium.

In those cases which are to receive intensive roentgen therapy, Martin and Moursund begin the use of vitamin B<sub>1</sub> orally two days preceding the first radiation treatment. We do not feel that such general prophylactic use of vitamin B<sub>1</sub> is indicated, since the symptoms are readily controlled by use of the hypodermic preparation, and since patients who develop irradiation sickness are definitely in the minority in comparison to the number of cases showing no ill effects from roentgen or radium

therapy. However, where interstitial radium element needles are used for cancer of the breast, there is as a rule an early and severe onset of anorexia, nausea, and vomiting, and the prophylactic use of vitamin B<sub>1</sub> may therefore be justified in these cases.

Further investigation of irradiation sickness, paralleled by daily or twice daily estimations of vitamin B<sub>1</sub> content in the blood serum, beginning two days before institution of radiation therapy, might be of scientific interest in the indication of a possible direct relationship between the actual level of vitamin B<sub>1</sub> and the onset of irradiation sickness.

#### CONCLUSIONS

1. Irradiation sickness is controlled rap-

idly and effectively by the administration of vitamin B<sub>1</sub> in large doses.

- 2. The hypodermic preparation of vitamin  $B_1$  gives more satisfactory results, and the amount required is usually only half that necessary when the drug is given orally.
- 3. Vitamin  $B_1$  therapy is most effective when daily doses are administered.

#### REFERENCES

- 1. Martin, C. L., and Moursund, W. H., Jr.
  Irradiation sickness. *Radiology*, 1938, 30, 277-281
- 2. Martin, C. L., and Moursund, W. H., Jr. Treatment of roentgen sickness with synthetic vitamin B<sub>1</sub> hydrochloride. Am. J. Roentgenol. & Rad. Therapy, 1937, 38, 620-624.
- 3. Sponheimer, K., Vitaminbehandlung von Strahlenschäden. Deutsche med. Wchnschr., 1938, 64, 1446–1447.



# EFFECTS OF ROENTGEN IRRADIATION UPON THE BLOOD VESSELS OF REPAIR TISSUE AND THE BROWN-PEARCE RABBIT EPITHELIOMA\*†

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THE PURPOSE of this study is to investigate the *in vivo* changes produced by a large single massive dose of roentgen radiation (10,000 r) upon the blood vessels, especially the capillaries of control and tumor sites. The Brown-Pearce rabbit epithelioma was transplanted in a modified Clark chamber<sup>6,14,28</sup> in the rabbit's ear in order that the sequence of these . changes might be followed under suitable magnification.15 Changes occurring in the smaller blood vessels immediately after the application of 10,000 r were striking and unexpected even with this large dosage. The grossly observable erythema appeared upon the fifth day, remained for the usual time, and did not seem atypical. While the magnitude of the changes noted in the finer structures is probably dependent to a great extent upon the dosage used, the sequence of events in the blood vessel damage is probably representative of the changes which occur with lesser dosage. Since these changes are of great interest to those engaged in tumor therapy they are reported in some detail.

Many observations have been made upon fixed tissues. 1,17,19,21,24,32 There are few data available concerning the effect of radiation upon the living, intact blood vessels in warm-blooded animals or human beings. A few observations upon the smaller vessels of the human skin have been described by David and Gabriel<sup>8,11</sup> and Siedamgrotzky, 29 who reported an increase in the number of end loops in the small vessels of the human skin during the erythema and changes in contractility of the larger vessels. Perfusion experiments

with rabbit's ears by Lazarew and Lazarewa<sup>18</sup> suggested that a hyperemia was present during the erythema stage. Most of the studies have been concerned with the grossly visible, erythema reaction. This visible reaction, with its peculiar time sequence described by Miescher<sup>22</sup> and Reisner<sup>26</sup> is little understood.

In the past two decades there has been a good deal of discussion concerning the effects of roentgen irradiation upon the blood vessels in and around the tumor mass. In 1904 Baermann and Linser<sup>2</sup> suggested that any destruction of irradiated tumors must depend upon primary vascular lesions and thus drew attention to degenerative changes in the intima of blood vessels accompanied by thrombosis. Bowen4 in 1903 found that complete obliteration of the blood supply to the tumor by surgical means resulted in mortification or gangrene, separation, and cure; while in 1936 Chambers and Scott,5 as a result of a series of exper ments started in 1932, declared that temporary obliteration of the blood supply (10t long enough to damage the blood vessels sufficiently to prevent a return or re-establishment of circulation) seemed to cause tumor regression. Woglom,33 in his 1922-1924 survey of the cancer problem. came to the conclusion that interference with blood supply was a factor in tumor regression. Ewing<sup>10</sup> in his 1925 Caldwell Lecture stated that "a large part of the destruct ve effect of roentgen rays upon tumors . . . is caused by interference with the blood and lymph circulation. There have been described rupture of capillaries, hemorrhage, thrombosis, com-

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pression of capillaries by exuded lymphocytes and plasma cells and growth of new connective tissue, swelling of all coats of large arteries, late arterial sclerosis, and the anemic condition of the radiation cicatrix." According to Cramer,7 all effects following irradiation are related to vascular stimulation and vascular degeneration, whereas Pullinger<sup>25</sup> declared that the causes of cell death in irradiated human tissue are due to an interruption of the blood supply through hemorrhage followed by organization, scarring, and pressure atrophy. Pack23 called attention to the fact that "in the case of many individual tumors the fundamental nature of the tissue of origin outweighs all other considerations when an attempt is made to estimate the radiosensitivity. Thus the primitive blood-forming tissues predetermine the radiosensitivity of tumors developing from their lymphoid, myeloid, and vascular derivatives." Pohle24 and others9 have had similar points of view.

Michels' 1935-1936 papers21 review the theories concerning capillary contractility and point out that from his experiments with a single massive dose of 400 r over the rabbit's abdomen the capillary endothelium of the mesentery seems to be relatively sensitive to irradiation since involution and sloughing of the emdothelial cells may occur with this dosage. This is accompanied by the loss of function of some capillaries. (See also refs. 16 and 32.) In 1936 Warren31 reviewed the work done up to that time on the physiological effects of roentgen irradiation upon normal body tissues and stated that the blood vessels seemed to be among the more radioresistant organs of the body.

It may be seen from the above brief summary that while the rôle of irradiation effects upon the blood vessels of a tumor is an important one, the sequence of events in vivo after irradiation is not known nor has the character of the changes produced been identified with any certainty.<sup>31</sup> It is possible that the simple rabbit ear cham-

ber<sup>15</sup> may introduce certain modifications in the tumor vessels, yet the vascular response to growth of the tumor transplant is so consistent as to make it seem an ideal subject for observation of the changes in the vessels in control and tumor tissues brought about by large single massive doses of radiation. Enough observations have been made upon the vascular pattern in control sites and tumor sites (150 animals) to warrant the statement that the observed changes are due to the radiation and do not depend upon any fortuitous circumstances.

#### APPARATUS AND METHODS

In previous experience with tumor transplants in the ear chambers of the rabbit in this laboratory, 15 it was obvious that many improvements had to be made in the lighting and arrangement of photographic equipment before photographic observation of tissues under the "window" could be accomplished with ease and accuracy. Considerable difficulty was also encountered in preparing a window of suitable shallowness which not only would allow good observation of blood vessel growth under high magnification but would also allow the tumor to grow to an appreciable physical size so that a pure "tumor vascularization" could be obtained in this acute type of experiment.

In the interests of compactness and ease in making observations through the window in the rabbit's ear, the conventional design for a photomicrographic apparatus<sup>12,13,20,27,30</sup> was abandoned in favor of a completely vertical arrangement. The source of light, condensing system, microscope and camera were centered along one axis and fixed accurately in position with the plane of the plate or film, the latter being parallel to the microscope stage holding the rabbit's ear (Fig. 1). The microscope and camera were physically separated to avoid the transmission of vibrations from the blower or the camera motor.

The focusing device used with the motion picture camera is different in that, unlike most of the current viewing set-ups, it does not employ a beam-slitting device and thus cause the loss of part of the light. The camera lens and the eyepiece of the microscope are both removed to avoid reflecting surfaces. By means of a lens-

mirror system the image is focused directly upon the film when the camera is in operation and on the shutter (which is painted white) when the camera is still. This enables the operator to focus carefully before starting the camera and then to "panoram" with ease, and to refocus for any slight variation in depth throughout the rabbit ear chamber thus maintaining the critical focus on the film. Changes in the light are easily noted and adjustments in exposure made as necessary.

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Since tungsten filament lamps of high wattage should not be burned horizontally, a compromise had to be made with regard to the light source. Therefore, the lamp socket was mounted so that the tungsten filaments were at a 45° angle with relation to the condensing system of the apparatus. This gave excellent illumination with maximum life of the bulb while eliminating one reflecting surface—the substage mirror of the microscope. A blower was used to cool the lamp. Neutral density filters (0.3, 0.6, 0.9) were used alone or in combination as protection for the eyes of the experimenter while locating fields in the operated area. Color filters were not used in the color photography of the thinner windows. A simple exposure meter was employed, the construction details of which are described elsewhere.3

A flat-topped animal board was constructed so that when the animal was placed on it comfortably in the prone position, 6.16 the ears were in a straight line level with the mechanical stage of the microscope, and complete mobility of the rabbit in a 150° radius with regard to the microscope was assured. By working at night in a quiet room with a trained rabbit and by avoiding fatigue of the rabbit, many psychic and other factors which might influence the reaction of the blood vessels were minimized. Patient and careful training of the rabbit is obviously essential to success with photography and observations under magnification.

#### PREPARATION OF WINDOW

The preparation of the window chamber is essentially the same as that previously reported except for certain improvements. A  $\frac{3}{8}$  inch nickel gromet and washer were inserted in the ear about 1.5 cm. from the tip and an aluminum templet used to establish the exact distance (1 cm.) from the gromet to the upper incision of the operated area. The gromet fits

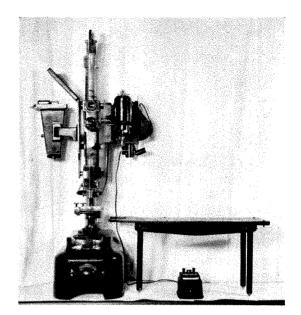


Fig. 1. This shows the microscope mounted on the heavy cast-iron base. The cameras are mounted on an old roentgen tube stand which contains a counterweight. The camera for still photographs is mounted on the left with the mirror at an angle above the ground glass to simplify focusing. The modified 16 mm. camera and driving motor are seen at the right. The camera lens is replaced by a constant viewing device containing a mirror and a built-in phosocell. The wire extends from this to the galvanometer on the table. The same leads may be conrected with the photocell built into the still camera, shown on the left. Either camera may be swung into place with ease. The special rabbit board is shown at the right of the base of the apparatus,

over a post soldered to the mechanical stage, thus fixing the position of the chamber under the microscope. Where stability is desired during examination of the operated field, this method of immobolization is simpler for this "acute experiment" than others requiring the exertion of pressure upon the ear, since normal circulation is not impaired.

The 1 sq. cm. skin area to be operated upon was then delineated and a scalpel nick made in the skin in one corner, and the skin stripped or rolled off with as little traumatization of blood vessels as possible (suggested by Dr. G. O'Hara). Stripping, rather than sharp dissection of the skin from both sides of the ear over this 1 sq. cm. area leaves intact the perichondrium with its blood vessels. Subsequent



Fig. 2. One day after operation. The dark areas outside of the central dense tumor mass are due to masses of red blood cells  $(60 \times)$ .

hemorrhage into the chamber, which was previously a handicap, was thus minimized.

Due to the short duration of this type of experiment a simple window was employed rather than the more complicated one necessary for the type of studies engaged in by Clark et al. Rectangles of cleared dertal x-ray film  $2\frac{1}{4}\times 1\frac{1}{2}$  inches, colored filter material (Blue No. 80), various grades of Kocapak (12×18 inch sheets), and cellulose acetate (20×50 inch sheets—thickness 0.0075 inch) were tried. The last was found most satisfactory for work requiring ordinary magnifications. For oil immersion examination, cellulose acetate (20×50 inch sheets—thickness 0.02 inch) with the center replaced by cover glasses fastened with collodion were used. The "window" was sterilized in alcohol before being used.

The sterile rectangular piece of cellulose acetate sheet to be used as a "window" was placed on either side of the ear overlapping the operated site and sewn in place, care being taken in sewing to avoid all visible blood vessels. The windows were then cut in situ so as to be roughly elliptical, thus avoiding trauma due to sharp corners. The area from sutures to window edge was covered above and below with collodion to provide an air-tight and fluid-tight seal.

Just before the last few stitches were made in the window of the rabbit's right ear, a very small piece of fresh, actively growing Brown-Pearce rabbit epithelioma was implanted, i.e., placed on the tissue of the "stripped" area just beneath the window. The left ear was treated in exactly the same manner except for the tu-

mor implant (which is omitted) since this ear was to be used as a control.

At the proper time after operation (ten to fifteen days) a dosage of 10,000 r including back-scattering was administered through a 5 cm. portal to the chamber areas of the right and left ears by means of a Machlett watercooled tube operated with no filter, full-wave rectification, 90 kv. (peak) (sphere gap), 17 ma, for 26.6 minutes at a target-mid-ear distance of 27.6 cm. For measurement, the middle of the ionization chamber was placed in air at the usual mid-ear position on the animal board at 27.6 cm. from the center of the target. The ionization chamber of the calibrated Victoreen r-meter was 1.2 cm, in diameter and the average thickness of the rabbit's ear in the operated area was 0.5 cm. including both cellulose acetate "windows." At the termination of the experiments the upper two-thirds of the ears, including the window area, were removed under general anesthesia and the specimens prepared (hematoxylin and eosin stain) for microscopic examination.

#### EXPERIMENTAL DATA

The following is a description of a typical experiment. Except for minor variations in the time relations, the results were identical for all 7 rabbits upon whom the roentgen irradiation was practiced. The stages of growth before irradiation are almost similar to the studies previously reported, <sup>15</sup> yet there are some additional details which differ because of the cham-

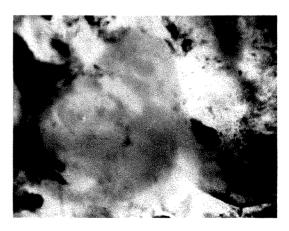


Fig. 3. Two days after operation. Punctate clumping on the left, near the tumor mass; a few vessels are seen elsewhere. A good many of the free red blood cells have disappeared (50×).

ber dimensions and the technique employed so that these are described:

#### Rabbit No. 95

(White, young, adult, male rabbit from tumor susceptible stock)
Weight=6 pounds.

2-I-38 16 days before operation Training period begun. Animal placed on board twice daily.

2-14-38 2 days before operation Hair removed from rabbit's ears in preparation for operation. Slight irritation of skin of both ears noticed.

2-15-38 1 day before operation Practically no irritation or erythema of skin of ears noticed.

2-16-38 Operation Window sewed in place Brown-Pearce rabbit epithelioma fragment placed under the "window" in the right ear. No Brown-Pearce rabbit epithelioma placed under the left (control ear).

2-17-38 1 day postoperative See Figure 2.

Tumor Implant: Some blood vessels show traumatic aneurysms. No neovascular response as yet. Clumps of red blood cells are spread throughout the chamber without clotting.

Control Chamber: Some instances of traumatic aneurysms noted. No neovascular response. Some clumps of red blood cells but no clotting.

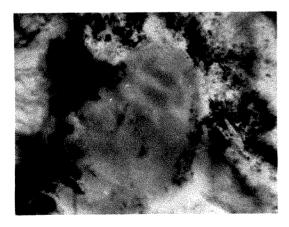


Fig. 4. Three days after operation. Note the vessels growing in from the sides especially on the left. The clumps of red blood cells are more sharply localized. A few are new  $(50 \times)$ .

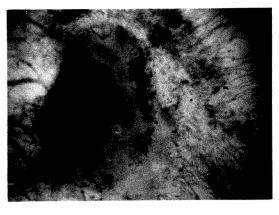


Fig. 5. Five days after operation. Well developed vascular supply and actively growing tumor spreading roost rapidly toward the right. The left border of the tumor is growing vertically (increasing thickness). Secondary punctate hemorrhages (probably the result of trauma) are noted on the right (50×).

2-18-38 Second day See Figure 3.

Tumor Implant: Eddy currents noted in the plasma and red blood cells suspension in vicinity of tumor implant. No change in size of tumor particle. No other changes noted except punctate clumping of red blood cells.

Control Chamber: No changes noted.

2-19-38 Third day

2-20-38

Fourth day

See Figure 4.

Tumor Implant: Numerous new small compact hemorrhagic areas seen surrounding tumor implant. No other changes visible.

Control Chamber: Diffuse clumps of red blood cells in the plasma still noticeable. No other changes noted.

Tumor Implant: Original hemorrhagic areas seem to be in the process of resorption. "End loop" formation noted as part of vascular pattern of new small vessels growing in the small compact clumps of red blood cells—toward the tumor and from the periphery of the operated area.

Control Chamber: No changes noted.

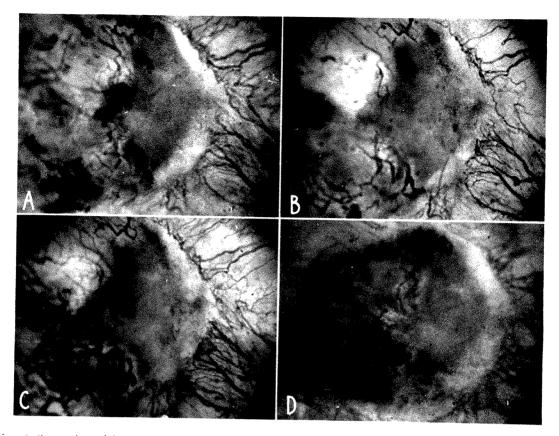


Fig. 6. Succession of changes over eight, nine, ten and twelve days after transplantation. The details of any plane are obscured by the thickness of the tumor growth. The centrifugal growth of the vessels is well shown at eight days, A. The great number of large and small vessels and the large amount of tumor slowly obscure the field (twelfth day, D). The roughly oval central dense mass represents the remnant of the original transplant which is well vascularized although the vessels are empty  $(50 \times)$ .

2-21-38 Fifth day Figure 5.

Tumor Implant. Original hemorrhagic areas seem to be almost totally resorbed. Slight increase in size of tumor fragment. A few new small hemorrhagic areas noted near growing edge of tumor fragment. A rich, seemingly haphazard growth of blood vessels from periphery of operated area is seen growing toward tumor fragment.

Control Chamber: Incipient vascularization evident at edges of operated are:

2-22-38 Sixth day Tumor Implant: Evidence of increased vascularization noticeable. Some sanusoid formation seen.

Control Chamber: Slow growth of blood vesses central from

2-23-38 Seventh day Tumor Implant: Second series of new vessel loops noted with blood vessels growing into tumor mass. There blood vessels seem to be growing in and the tumor edge seems to be growing out. Growing edge of tumor fragment partially sur-

periphery of operated control

growing out. Growing edge of tumor fragment partially surrounded by punctate hemorrhagic areas.

Gontrol Chamber: Continued slow growth of blood vessels centrad

area.

growth of blood vessels centrad from periphery of operated area. Blood vessels now one-third of distance from periphery to center of operated area.

2-24-38 Eighth day

See Figure 6.

Tumor Implant: Tumor fragment increasing in size and changing

from pear-shape to an elliptical one. Some of the former small new vessels have increased in size and many of the smaller vessels have entirely disappeared.

Control Chamber: Little change noted.

See Figure 6.

2-25-38 Ninth day

Tumor Implant: Some slight resorption of punctate hemorrhages. Steady but rather slow growth of blood vessels and tumor edge.

Control Chamber: Slow growth of blood vessels centrad, now almost one-half of distance to center of chamber.

2-26-38 Tenth day See Figure 6.

Tumor Implant: Increase in size and decrease in number of filled blood vessels going to and from tumor fragment continues.

Control Chamber: Little change noted.

2-27-38 Eleventh day

Tumor Implant: Vascular pattern about tumor seems fairly well settled. Little change from previous day as to size or arrangement of blood vessels evident. Hemorrhagic areas clearing slowly. Chamber now nearly filled with tumor mass. Tumor almost a spheroid and expansion and vascularization almost (but not quite) at a standstill.

Control Chamber: Little change noted.

2-28-38 See Figure 6. Twelfth day Tumor Imp

Tumor Implant: Rupture (? trauma) of endothelial tubes of new growing capillaries with hemorrhage without clotting noted. Tumor and blood vessels growing slowly but steadily with little change in vascular pattern now as compared with active proliferation, alteration, and disappearance of some of the vessels seen during the first ten days of tumor growth.

Control Chamber: Little change noted except continued slow growth of blood vessels centrad from the periphery of the operated area and the gradual resorption of punctate hemorrhagic areas. 3-1-38 Thirteenth day Tumor Implant: Large, thinwalled blood vessels (obviously capillaries of a sinusoidal type) make readily visible various phenomena such as reversal of flow, "plasma skimming" (a process which brings about a reduction in the number of red blood cells and may even cause their entire disappearance from a certain capillary field), true "stasis" with consequent packing of red blood cells in capillaries, passive diapedesis, and active penetration of endothelial walls by wandering white cells. The chamber is almost ready for irradiation.

Control Chamber: Little change noted.

3-2-38 Fourteenth lay Tumor Implant: All traces of hemorrhage originally seen in tumor chamber have disappeared and the punctate secondary hemorrhagic areas are scarcely noticeable. Tumor has been changing by degrees from an elliptical to a spherical shape but the vascular pattern has remained essentially the same for the past four days (Fig. 7 A).

Control Chamber: The blood vessels have continued to grow slowly from the periphery of the operated area toward the center and have now almost filled the area (Fig. 7 B).

3-3-38 Irradiation

Tumor Implant: Irradiated tumor with 10,000 r without trauma. One-half hour after irradiation was completed (Fig. 7 D and G), a slight reddish haze was noted under various magnifications. It was impossible to tell whether this was due to a diffuse spread of the red blood corpuscles throughout the area or to hemolysis. This color change was not due to any change in the volume of blood present in the vessels (which continued unchanged but seemed to be due to extravascular change).

Control Chamber: A haze similar to that in tumor implant chamber also noted in control ear which also received 10,000 r as described in the Method.

3-4-38 1st day after irradiation Tumor Implant: Increase in extravascular red haze noted (Fig. 7 E and II). Many vessels are beginning to assume a "beaded" appearance. This seems to be only a local small expansion or shrinkage and if anything the blood flow seems less. No noticeable change in the normal functional behavior of capillaries could be seen at this stage, however.

Control Chamber: Increase in red haze noted here also, as well as the above-mentioned "beaded" appearance. No change in the normal functional behavior of the capillaries could be seen.

3-5-38 2nd day after irradiation Tumor Implant: Reddish haze noticeable but seems less marked. Tumor seems to be shrinking in size although the outlines are difficult to see.

Control Chamber: Reddish haze noticeable here also, interfering with observation of some of the blood vessels.

3-6-38 3rd day after irradiation Tumor Implant: Reddish haze clearing. Flow of blood in vessels seems sluggish but vessels themselves appear to be more normal in contour. Emptying and filling seem to go on as usual.

Control Chamber: The blood vessels in the control chamber seem to be behaving in like manner to those in the tumor implant chamber.

3-7-38 4th day after irradiation Tumor Implant: A secondary red haze has developed which seems to be more marked than the immediate reaction. Observation and photography have become difficult due to loss of contrast as a result of absorption of the various wave lengths of light by the reddish

haze throughout the chamber. Many blood vessels are beginning to shrink and remain empty. Some have broken up with small diffuse hemorrhages along their course while others have a thin, crinkly or tortuous course with little blood flow. Destruction of vascular pattern seems imminent in patches in different portions of the tumor chamber. The actual blood flow or total contained volume in the irradiated areas seems actually diminished.

Control Chamber: Results similar to those obtained in the tumor implant chamber, were also noted in the control area.

Tumor Implant: Chamber is so obscured by the diffuse haze (red) that observation and photography were impossible. This red haze was grossly visible for the first time since irradiation. Blood vessels were broken down and the tumor seemed to be shrinking due perhaps to resorption.

Control Chamber: Vascular pattern in the control area seemed to be destroyed. None of the former landmarks remained visible.

3-15-38 12th day after irradiation

3-8-38

5th day after

First notice-

irradiation

able gross

ervthema

Chambers have failed to clear. No change from above. Gross erythema marked, Observation and photography impossible. Pictures of the whole ear showing the chamber in situ taken in color. Then the upper two-thirds of each ear was removed for microscopic study.

The rabbits in all seven of these experiments were all refractory to subsequent re-inoculation with tumor in the testicle. This was a common finding (70 per cent) following spontaneous

Fig. 7. Sequence of events following single massive dose of 10,000 r. A, low power (10×) view of the tumor fifteen days after transplantation just before irradiation. The tumor is spherical and well vascularized. B, control area (10×) fifteen days after operation showing almost complete healing and normal arborization of the vessels. C (40×). Vessel pattern at the margin of the tumor just before irradiation. D, the same field one-half hour after irradiation showing development of red haze around the vessels. E, the same field one day after irradiation showing marked increase in the red haze (which almost amounts to microscopic bleeding). Many of the vessels are empty. E, higher power of E before irradiation showing an anastomotic loop of a small vessel with its capillary branches (90×). E, same loop one-half hour after irradiation showing the red haze which has developed around the vessels (same as E). E0, same loop one day after irradiation showing the marked increase in the haze and the reduction in the blood flow (same as E1 (90×).

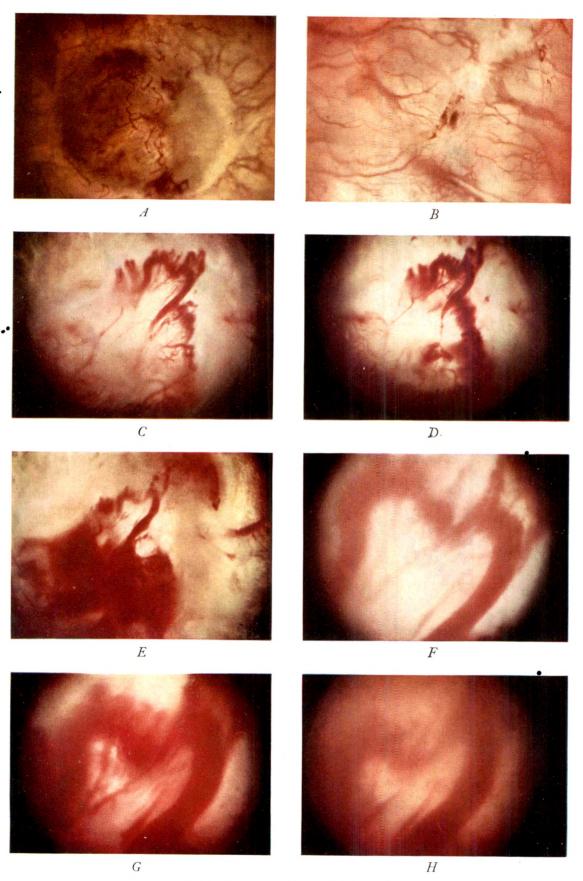


Fig. 7 (See explanation on facing page)

resorption of the tumor without irradiation in these ear chamber experiments.<sup>15</sup>

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## EXAMINATION OF MICROSCOPIC SECTIONS THROUGH THE EAR CHAMBER

- 1. Non-irradiated Control Ear Chamber One Month after Operation, No. y 181. This shows the site of operation healed, with both sides immediately beneath the window covered by a thin, yet well developed epithelial layer. There is some formation of a definite corium although the age of this preparation is not sufficient to allow for the development of much thickness. There is a well defined basal layer, the nuclei of which show a fairly large number of mitotic figures. The subcutaneous tissue is rich in capillaries and blood vessels of various sizes. The larger ones show evidence of the development of a muscular wall. Hair follicles and glandular structures have reappeared near the margin of the repair area. The staining of all nuclear structures is essentially normal.
- 2. Non-irradiated Tumor Implant Ear Chamber, One Month after Operation, No. y 727. The site of operation is covered with a thin layer of epithelium but this is, however, one or two cells thicker than that of the control site. The number of blood vessels in the tumor implant site is many times greater than that of the control. These vary greatly in size and the greater majority are only endothelial tubes. Spread in among the small capillary meshworks are the shadows and debris of the tumor cells. No actively growing or definitely viable tumor cells are found. Aside from the pallor of the degenerating tumor cells, the staining of the cells in the section is normal. In some sections viable appearing tumor cells with mitotic figures are seen. This variation in the tumor is commonly found at this stage (resorption stage).
- 3. Irradiated Control Ear Chamber, No. y 175, Forty-three Days after Operation, One Month after Irradiation. The structure here is exactly the same as the control in the number of vessels, thickness of epithelium, and organization of the connective tissue. In general all of the cells are pale, poorly stained, and ill defined. The nuclear chromatin, particularly of the basal layers of the skin, is clumped and there are large pale areas in the nucleus which take a slight eosinophilic tint. The nuclear outlines are not sharp or well-defined. The connective tissue fibrils are slightly swollen and fuzzy.

They are more widely separated than usual suggesting an increase in intercellular fluid. The endochelium in the larger vessels is crinkly and their cell nuclei are somewhat swollen and stain poorly. In some cases the endothelial nuclei seem to have lost their chromatin structure leaving a dark, hazy remnant. The membrane-like endothelial wall is extremely thin (almost filamentous). Elsewhere are seen irregular collections of endothelial cell debris suggesting the site of a small blood vessel. Intermingled with this debris and nearby are frequently noted small orange-colored collections of amorphous material and shadows of red blood cells. No thrombi are noted. Polymorphonuclear and other phagocytic cells are more numerous than normal, especially in the neighborhood of disorganized blood vessels. Occasionally these cells are apparently adherent to the wrinkled endothelial walls. The nuclear material in the cartilage is likewise hazy, poorly stained, and a little swollen but seems otherwise unchanged.

4. Irradicted Tumor Site, One Month after Operation; Twenty-one Days after 10,000 r. No. y 174. The same general pallor and indefinite outline are visible as in the irradiated control site; the same damage to the endothelium and the same masses of red blood cells in various stages of disintegration outside of the vessels. These extravascular collections of the red blood cells are more numerous in the tumor site than elsewhere. The tumor site is occupied by a few dim shadows of tumor cells in all stage of disintegration. Organized clotting or thromboses are not seen. No tumor cells can be clearly seen and there are no mitoses. In some places the vessel pattern is very much like that seen in vivo with large numbers of parallel branches of small vessels almost in contact with each other because of the dissolution and disappearance of the tumor cells. There is less evidence of the presence of tumor in these sections than in the unirradiated resorption stage of the same age, probably as a result of its rapid dissolution following the gradiation.

#### DISCUSSION

In general, the development of the vascular reactions taking place in the normal control area corresponds closely to those reported by the Clarks and their coworkers and to the previous experiments in this laboratory.<sup>6,15</sup> The presence or absence of tumor in the right ear seemed to have no effect upon the vascular reactions of the left (control) ear. Slow progressive repair with gradual vascularization central from the periphery of the operated areas was noted in all cases, with less profusion of capillary growth in the control sites as compared with vascularization in the tumor implanted chambers.

Efforts were made to observe the changes in frequency and the extent of the normal periodic filling and emptying of the capillaries in the control areas and the tumor growth ears, but no periodicity was noted. The mechanism controlling these erratic changes in blood flow was not apparent.

Perhaps partially due to the difference in operative technique and chamber size and partially to the lessening in growth rate of the present tumor in comparison with the tumor in former years, sinusoid formation was practically negligible at the periphery of the growing implant. In fact, all of the capillaries both in normal repair areas and in tumor implanted areas seemed to be of somewhat smaller caliber than those photographed by Ide et al. 15 Postoperative hemorrhage and secondary hemorrhage occurred in the normal repair area but with less severity than in the areas in and surrounding the tumor. This was probably due to the relatively large size and greater number of fragile vessels in the tumor. Corona-like vascular arrangement around the tumor edge and a definite change in direction of the blood vessels from a centrad to a peripheral direction, due possibly to the centrifugal direction of peripheral tumor growth, was noted as before. Since there was no change in vascular response in either the control or tumor implant sites from that previously reported,15 abnormalities described after irradiation were probably due to the effects of the irradiation. These changes are probably not specific for roentgen irradiation alone, but may in whole or in part be noted after other types of injury (ultraviolet, heat, chemical, etc.).

The almost immediate development

(within one hour after irradiation) of a diffuse redness around the blood vessels was unexpected since no gross change could be noted in the vessels and the walls of the capillaries showed no visible patencies. However, a transitory erythema or blushing has been reported clinically to occur within the first four to twelve hours after large single massive dosage. In view of the observations of Michels and a study of our own fixed sections, it seems likely that this diffuse redness around the blood vessels is due to the extravasation of erythrocytes and plasma from the blood vessels through the damaged endothelium. Under the present circumstances it is impossible to say whether the endothelial cells contract away from each other, or become torn and fragmented as an acute reaction to the irradiation. The bead-like appearance of the capillaries shortly after irradiation might indicate a considerable direct effect of the radiation upon the endothelial cells while the complete breakdown of the vascular pattern within a week after irradiation leaves little doubt that such is the case.

As a result of these observations, there seems little doubt concerning the validity of the contention of many experimenters that primary damage to the blood vessels is an important factor in radiation effects upon tumors. Since the changes described above occur in the blood vessels of both the control and tumor tissues this effect upon the endothelium is not influenced by the tumor. There are innumerable observations reported (mainly histological) upon the direct effects of radiation upon the tumor cells. It is obvious from these observations that the part played by the changes in the blood vessels may have immediate summative effects as well as lasting summative effects upon tumor growth and survival.

We realize that 10,000 r is a high massive dose, yet in experiments being carried on in this laboratory by Dr. Sidney Larson (unpublished) *in vivo* massive dosage of this amount has not always been lethal for this

tumor. The dosage is large enough, however, to yield pronounced blood vessel effects. The effects of smaller doses (massive and fractional) will be reported later.

The failure of a gross erythema to appear within the first five days and its sudden appearance and progression from this time on is probably related to the fact that the endothelium in general retains its integrity and tonus up to the fifth day. After this, a general dissolution of capillary structure begins with rapid diffusion of red blood cells and plasma into the tissues nearby. This is followed by a slow recovery of tone in portions of the wall which results in the beaded, crinkly appearance noted above. About this time blood flow reappears in the •larger vessels although the flow never regains its normal volume during the period of observation following irradiation (twelve to fourteen days). Many vessels are not filled again so the tumor cells supplied by them must, of necessity, remain dormant or die even if they may not be directly damaged by the irradiation. The ervthema (gross) is thus an extravascular manifestation rather than being due to an increased blood flow in the vessels themselves or an increased number of patent vessels.

#### SUMMARY AND CONCLUSIONS

- 1. Actively growing Brown-Pearce rabbit epithelioma with well established circulation in the tumor ear chamber, and the control ear chamber, were irradiated with 10,000 r and the *in vivo* reaction of the blood vessels studied in seven rabbits.
- 2. Almost immediately after irradiation (within an hour) a red haze developed around both the tumor and control vessels which became progressively more marked microscopically but the gross erythema did not appear until the fifth day after irradiation. At this time the tissues were so obscured by the diffuse redness (extravascular red blood cells) as to make further microscopic study impossible.
- 3. Within a few days after irradiation the blood vessels in the tumor and control sites became beaded and irregular in con-

- tour. The flow was restricted and erratic, many vessels remaining empty. The normal responses to paling and flushing were almost intact.
- 4. By the end of the fifth day after irradiat on a gross erythema developed and the finer details were obscured. Blood vessel and capillary dissolution began at this time with a slow recovery over the following week. Many large vessels (as well as small ones) never refill with blood after this
- 5. Although the erythema is a direct result of damage to the blood vessel endothelium by the irradiation, the color is due to the presence of red blood cells in the perivascular structures. The redness does not become visible to the eye until a large amount of blood has collected in the extravascular spaces due to vessel dissolution.
- 6. The reaction in the endothelium from the irradiation is the same in both the control and tumor vessels so that the tumor growth does not change the endothelium in this regard even though it calls forth a more active vessel proliferation than does the repair reaction.
- 7. All seven of the animals developed refractory states to re-inoculation after the destriction of the tumor by the irradiation.

#### REFERENCES

- BACHEM, A Physical and biological observations about skin reactions. Radiology, 1927, 9, 241– 250.
- 2. BAERMANN, G., and LINSER, P. Ueber die lokale und allgemeine Wirkung der Röntgenstrahlen. München. med. Wehnschr., 1904, 51, 996-999.
- 3. Bishop, F. W. Exposure meter for cinephotomicrography and still photomicrography. *Science*, 1,38, 87, 239-240.
- Bowen, W. H. Effects of surgical interference with blood supply on growth of transplanted carcinomata and sarcomata. Third Scientific Report, Imperial Cancer Research Fund, 1908, p. 126.
- 5. Снамвет, А., and Scott, G. M. On the effect of a temperary stoppage of blood supply of rat tumous. У. Path. & Bact., 1936, 42, 265-269.
- CLARK, E. R. Observations on living growing lymphatics in tail of frog larva. Anat. Rec., 1909, 3, 183-198.

- CLARK, E. R., KIRBY-SMITH, H. T., REX, R. O., and WILLIAMS, R. G. Recent modifications in method of studying living cells and tissues in transparent chambers inserted in rabbit's ear.

  Anat. Rec., 1930, 47, 187-211.
- CLARK, E. R., HITSCHLER, W. J., KIRBY-SMITH, H. T., REX, R. O., and SMITH, J. H. General observations on ingrowth of new blood vessels into standardized chambers in rabbit's ear, and the subsequent changes in the newly grown vessels over a period of months. *Anat. Rec.*, 1931, 50, 129–167.
- CLARK, E. R., SANDISON, J. C., and Hou, H. C. New rabbit board for use in studying living tissues in transparent chambers introduced into ear. *Anat. Rec.*, 1931, 50, 166–173.
- CLARK, E. R., and CLARK, E. L. Observations on living preformed blood vessels as seen in transparent chamber inserted into rabbit's ear. Am. J. Anat., 1931–1932, 49, 441–474.
- CLARK, E. R., CLARK, E. L., and SWENSON, E. A. Contraction of arterioles of various sizes and the passivity of venules and capillaries. *Am. J. Physiol.*, 1933, 105, 19-20.
- CLARK, E. R., and CLARK, E. L. Evidence relating to removal of extravascular substances without the agency of lymphatic vessels. *Am. J. Physiol.*, 1933, 105, 19.
- CLARK, E. R., and CLARK, F. L. Observations on lifing arterio-venous anastomeses as seen in transparent chambers introduced into rabbit's ear. Am. J. Anat., 1934, 54, 229-286.
- CLARK, E. R., CLARK, E. L., and WILLIAMS, R. G. Microscopic observations in living rabbit of new growth of nerves and establishment of nerve-controlled contractions of newly formed arterioles. Am. J. Anat., 1934, 55, 47-77.
- CLARK, E. R., and CLARK, E. L. New formation of arterio-venous anastomoses in rabbit's ear.

  Am. J. Anat., 1934, 55, 407-467.
- CLARK, E. R., and CLARK, E. L. Observations on changes in blood vascular endothelium in living animal. *Am. J. Anat.*, 1935, 57, 385-438.
- CRAMER, W. Experimental observations on • therapeutic action of radium. Scient. Rep. Invest. Imp. Cancer Research Fund, 1932, 10, 95-123.
- 8. David, O. Untersuchungen über den Einfluss von Röntgenstrahlen auf Kapillaren. Strahlentherapie, 1926, 23, 366-368.
  - DAVID, O. Examination of effect of roentgen rays on blood vessels and capillaries. *Brit.* J. *Radiol.*, 1925, 30, 462-464.
  - David, O., and Gabriel, G. Die Kapillarmikroskopie des Röntgenerythems. Strahlentherapie, 1923, 15, 125–145.
  - David, O., and Gabriel, G. Die Kapillarmikroskopie des Röntgenerythems. 11. Strahlentherapie, 1923–1924, 16, 372–380.

- DAVID, O., and GABRIEL, G. Kapillarmikroskopische Untersuchungen über die Tiefenwirkung von Röntgenstrahlen. Strahlentherapie, 1924, 17, 192–196.
- DESJARDINS, A. U. Classification of tumors from standpoint of radiosensitiveness. Am. J. ROENTGENOL. & RAD. THERAPY, 1934, 32, 493-499.
- 10. Ewing, J. Tissue reactions to radiation. Am. J. Roentgenol. & Rad. Therapy, 1926, 15, 93-115.
- II. Gabriel, G. Die Beeinflussung von Tierorganen durch Röntgenbestrahlung. Strahlentherapie, 1926, 22, 107-124.
- 12. Graton, L. C., and Dane, E. B., Jr. A precision all-purpose microcamera. J. Optical Soc. America, 1937, 27, 355.
- 13. HARDY, A. C., and PINEO, O. W. A simple cinephotomicroscopic apparatus. J. Soc. Motion Picture Engineers, 1931, 17, 216.
- 14. Hou, H. C. Behavior of adrenal transplants in transparent chamber inserted into rabbit's ear. *Proc. Soc. Exper. Biol. & Med.*, 1929, 26, 745-747.
- 15. IDE, A. G., BAKER, N. H., and WARREN, S. L. Vascularization of the Brown-Pearce rabbit epithelioma transplant as seen in the transparent ear chamber. Am. J. ROENTGENOL. & RAD. THERAPY, Dec., 1939, 42, 891-899.
- 16. Krogh, A. Anatomy and Physiology of Capillaries. Second edition. Yale University Press, New Haven, Conn., 1930.
- 17. KÜSTNER, H. Die Dosierung in der Hauttherapie. Fortschr. a. d. Geb. d. Röntgenstrahlen (Kongresshft.), 1932, 46, 78-81.
- LAZAREW, N. W., and LAZAREWA, A. Ueber die funktionellen Veränderungen der Blutgefässe nach Röntgenbestrahlung. 1. Strahlentherapie, 1926, 23, 41-78.
- 19. Lewis, W. H. Vascular pattern of tumors. Bull. Johns Hopkins Hosp., 1927, 41, 156-162.
- LOVELAND, R. P. An apparatus for motion photomicrography on 35 mm. film. J. Optical Soc. America, 1932, 22, 161.
- 21. MICHELS, N. A. The plexus omentalis and its relation to capillary innervation in omentum of rabbit. *Am. J. Anat.*, 1935, 57, 205-258.
  - MICHELS, N. A. Medullary and non-medullary erythropoiesis with special reference to plasma-cell erythrophage or Russell body cell, and to erythrocatheretic (erythrolytic) function of lymph nodes and hemal nodes. Am. J. Anat., 1935, 57, 439-501.
  - MICHELS, N. A. Structure of capillaries and the unmyogenic character of Rouget cells (pericytes) in omentum of rabbits and in the web of living frogs. *Anat. Rec.*, 1936, 65, 99-125.
- 22. MIESCHER, G. Das Röntgenerythem. Strahlentherapie, 1924, 16, 333-371.
  - Miescher, G. Röntgenbiologie der gesunden

- und kranken Haut. Strahlentherapie, 1927, 27, 257-280.
- MIESCHER, G. Carcinomtherapie mit superponierten (verzettelter) Röntgenbestrahlungen. *Strahlentherapie*, 1930, 36, 434–471.
- 23. PACK, G. T. Principles governing the radiation therapy of cancer. Am. J. ROENTGENOL. & RAD. THERAPY, 1936, 36, 233-244.
- 24. Pohle, E. A. Clinical Roentgen Therapy. Chap. 11. Lea & Febiger, Philadelphia, 1938.
  - Pohle, E. A., and Bunting, C. H. Studies of effect of roentgen rays on liver; histological changes in liver of rats following exposure to single graded doses of filtered roentgen rays. *Acta radiol.*, 1932, 13, 117–124.
- 25. Pullinger, B. D. Causes of cell death in irradiated human tissue. J. Path. & Bact., 1932, 35, 527-540.
- Reisner, A. Untersuchungen über die Veränderungen der Hauttoleranz bei verschiedener Unterteilung der Strahlendosis. Strahlentherapie, 1930, 37, 779-787.
  - Reisner, A. Hauterythemverlauf bei fraktionierter Verabfolgung grosser Strahlenmengen. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1932, 45, 293–307.
- ROSENBERGER, H. Micro-cinema in medical research. Tr. Soc. Motion Picture Engineers, 1927, 11, 750.
  - ROSENBERGER, H. Standard microcinematographic apparatus. Science, 1929, 69, 672.
- 28. Sandison, J. C. New method for microscopic

- study of living growing tissues by introduction of wansparent chamber in rabbit's ear. *Anat. Rec.*, 1924, 28, 281–287.
- Sandmon, J. C. Transparent chamber of the rabbit's ear. Am. J. Anat., 1928, 41, 447-473.
- Sandbon, J. C. Method for microscopic study of growth of transplanted bone in transparent chamber of rabbit's ear. *Anat. Rec.*, 1928, 40,
- Sandison, J. C. Contraction of blood vessels and observations on circulation in transparent chamber in rabbit's ear. *Anat. Rec.*, 1932, 54, 105-127.
- 29. SIEDAMGROTZKY, K. Ueber der Verhalten der Hautkapillaren im Röntgenbestrahlten gebiet *Strahlentherapie*, 1925, 19, 84–123.
- 30. TUTTLE, C. Motion photomicrography with cine-kodak. Tr. Soc. Motion Picture Engineers, 1927, 11, 213.
- 31. Warren, S. L. Physiological effects of roentgen radiation upon normal body tissues. *Physiol. Rev.*, 1928, 8, 92–129.
  - WARREN, S. L. Biological Effects of Radiation. Duggar. McGraw-Hill, 1936, Chap. XIV, 473=539.
- 32. WEYRAUCH, H. B., and DE GARIS, C. F. Normal and interrupted vascular patterns in intestinal mesentery of the rat; experimental study on collaberal circulation. Am. J. Anat., 1937, 61, 343-372.
- 33. Woglo-4, W. H. A critique of tumor resistance. J. Cærcer Research, 1922, 7, 283-301.



# THE EFFECT OF ROENTGEN RAYS UPON BACTERIOPHAGE

#### STUDIES IN BACTERIAL METABOLISM. CXI

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**HE** discovery by Roentgen that x-rays will penetrate deeply into living tissues and make visible denser structures, as bones, and reveal imbedded foreign bodies as missiles of warfare very naturally attracted attention to the possibility of utilizing these rays in treatment of microbic infections of the body. Some promising clinical results have been reported, and, logically, attempts have been made to correlate these with direct effects of roentgen rays upon naked bacteria, viruses and substances of bacterial origin without intervention of cellular structures. Judging from the literature it may be said that the results of such direct exposure of bacteria and viruses to roentgen rays and even to radium emanation have been disappointing in general. Bacteria and viruses do not appear to be harmed materially even after exposures that would be unendurable by the human body. It would seem from these experiments that the smaller the biological particle exposed to roentgen-ray bombardment, the less effective is its action upon each exposed unit. Several theories have been advanced to account for this noteworthy contrast between facile tissue penetration by roentgen rays and their microbicidal ineffectiveness. Perhaps the most widely accepted of these is the "target" theory, stated by Mohler and Taylor8 thus: "The effects of x rays in liquids are localized in 'columns of ionization' along the path of each high speed electron. It is assumed that biological effects are produced in these col umns. Cathode rays of 155KV give an area of  $0.68 \times 10^{-10} \text{cm}^2$ : x rays of wave lengths 0.56 to 4 Ångstroms\* give values (areas) between 0.72 and  $1.6 \times 10^{-10}$  cm<sup>2</sup>. A particle 0.2 microns in diameter has a 50-50 chance

of escaping a dose of 100 r. Ultramicroscop-

ic particles have an even chance of escaping a dose of 1,000,000 r. The passage of a

"column of ionization" (the path of an elec-

tron) through a bacillus is in general nonfatal: the column must pass through a particular point to cause death<sup>11</sup>.† Crowther<sup>4</sup> has developed this "target" theory somewhat in greater detail. He states: "The beam of x rays consists of a swarm of protons. The energy of each proton is proportional to the voltage at which it is excited." This theory reëmphasizes the discontinuous nature of roentgen-ray emission and assumes that action takes place whenever a biological structure (bacterium or phage particle for example) is hit by radiation. "A hit is registered whenever a pair of electrons is produced anywhere within the sensitive particle." According to this "target" theory microscopic particles have a very fair chance of escaping the effects of radiation simply owing to the (relatively) wide distances which separate points at which energy is concentrated. Therefore it would appear that missing the "target" is a prime cause for failure of roentgen-ray bombardment of particles of small size (bacteria or phage) rather than insufficient energy or unsuitable state of the projectiles to inflict damage "since a single quantum of x ray radiation has sufficient energy to produce some hundreds of ions in tissues in which it is absorbed." The tenability of the "target" theory lies in a tacit admission that roentgen rays are physically capable of producing lethal effects in microscopic and submicroscopic biological entities even if their full effectiveness is never realized because of the (mathematically) inherent

<sup>\*</sup> An Ångström unit is 10-8 cm.

<sup>†</sup> For a more complete discussion of the mathematics involved in the "target" theory see Pugsley, Oddie and Eddy.9

large proportion of "misses" (and possibly ineffective, glancing blows). One weakness of the "target" theory is its failure to recognize that "misses" which explain failures logically postulates "hits" which imply successes, if the roentgen-ray bombardment could be made sufficiently dense or accurate to insure that each bombarded particle should eventually be in position to receive a direct hit. However, the experimental difficulties of producing convincing proof, if any, of inaccuracy of the mathematical assumptions involved puts the burden of proof on the opposition.

Bacteriophage, regarded by many observers a member of the group of filterable viruses, possesses several characteristics peculiarly favorable for experimentation with roentgen rays. It is filterable; it is produced only in presence of living cells; it is exquisitely species specific. Also it can be generated consistently without use of experimental animals. It is extremely potent and its potency can be measured by the dilution method in multiples of 10. Finally, it is inactivated by physical or chemical agents, and inactivation proceeds progressively.

The published literature on the effects of roentgen rays on bacteriophage is scant. Mizuno, however, made extensive comparative studies of the effects of roentgen rays and of ultraviolet radiation upon phage. He states that roentgen rays, unlike ultraviolet radiation, have no appreciable effect upon bacteriophage. Beckwith, Olson and Rose<sup>1</sup> found that bacteriophage exposed to roentgen rays at a distance of 30 inches was little changed even after relatively long exposure. Wyckoff<sup>13</sup> expressed the view that the lethal effects of roentgen rays and of ultraviolet radiation were not the same. Wright and Kersten<sup>12</sup> state that soft roentgen radiation (at 1.54 and 1.38 A) had little effect on phage after one hour's exposure, but that after five to six hours' exposure the effect was somewhat greater. Even after long exposures of bacteriophage to radium emanation little or no lethal effect is noticed. Bruynoghe and Mund<sup>2</sup> kept

typhoid phage in contact with 7-8 millicuries of radium emanation for five days without detecting loss of titer and Spencer<sup>11</sup> found that certain bacteria were resistant to radium emanation. The general impression held at present appears to be reflected in the observations of Schepmann and Flecke<sup>10</sup> who state that the longer (softer) roentgen rays are more effective lethally than the shorter (harder) roentgen rays. Equal doses of hard rays produce only half the effects of soft rays upon cultures of staphylococcus, B. coli, B. pyocyaneus, B. prodigiosus and B. mesentericus. (See also Pugsley, Oddie and Eddy9.) The statement made by Kaye6 several years ago is significant: "Curiously enough the rays (x rays) have little effect or no effect on bacteria or their spores, and in this respect stand out in marked contrast to ultra-violet light.'

#### EXPERIMENTAL

a. Bacteriophages Used in These Investigations. "Pure' bacteriophages, that is phages freed from practically all associated protein-like substances and containing about 0.5 mg. nitrogen per 100 cc. were prepared, according to the procedure of Colwell, for B. coli, Flexner and for Staphylococcus aureus. These phages were suspended in distilled water and filtered through Berkefeld filters. Their titer was 10-8; that is to say, they contained 100,000,000 phage particles per cubic centimeter. They retained this tiper during the entire time of experimentation.

b. Technique of Exposure of Bacteriophages to Roentgen Rays. The phages were exposed in uncovered Petri dishes (of Pyrex glass) in layers 0.6 cm. deep. The total volume was 20 cc. The Petri dishes were placed exactly 12 inches from the cathode. The energy output of the roentgen machine was determined accurately for this distance. It was 20,000 r in twenty-five minutes. A photographic plate exposed at this distance showed that the area of maximum emanation covered a circle 6 inches in diameter. Outside this circle the intensity of emanation diminished considerably. Inasmuch as the diameter of the Petri dish which contained the phage was 4 inches, and the dish was accurately centered for each exposure, the full force of the roentgen ravs should have been received by the phage each time. No detectable rise in temperature was noted during exposures. The duration of exposures was from ten to thirty minutes—8,000 to 24,000 r. Phages in open Petri dishes were the controls, unexposed to roentgen rays. After exposure the phages were filtered to eliminate possible incidental contaminants. The filtrates were then tested for potency in the usual manner by serial dilution in multiples of 10.

c. Rotation of Bacteriophage. Having in mind the "columns of ionization" referred to above. an attempt was made to increase the chances of "hits" by rotating the Petri dishes within the area of greatest intensity of emission eccentrically (1 cm. off center) on a slowly turning phonograph disk rotator, during the entire time of exposure. By so doing it was hoped (remotely) that the effects of these "columns of ionization" might be increased in the aggregate through reduction of the chances of "misses"that is to say, futile bombardment of empty areas—and that the existence of these columns might be inferred by a difference in titer between phages exposed to bombardment, still and rotated respectively. These phages were water clear and therefore the shielding effect of alien substances was minimal. There should be little protective action of one phage particle for another over a period of thirty minutes (the time of maximal exposure). Each of the 100,-000,000 phage particles in each cubic centimeter of solution exposed to the roentgen-ray bombardment should have ample opportunity to be hit at least once. Finally, the method of serial dilution, titrated in multiples of 10, is sufficiently precise to register inactivation of a significant number of phage particles.

#### RESULTS

The results of exposure of several "pure" bacteriophages, including both separate species and separate preparations of each species of phage, to the action of roentgen rays (24,000 r during thirty minutes' exposure) were negative. The titer of the phages, rotated or unrotated, was not significantly reduced. It is worthy of note that the glass of the Pyrex Petri dishes was permanently browned as a result of these exposures. In light of the rapid and complete inactivation of these same phages ex-

posed to ultraviolet radiation, reported elsewhere, the conclusion is drawn that roentgen rays (24,000 r in thirty minutes) have no significant effect upon bacteriophage.

#### DISCUSSION

The results of these experiments are in accord with those of other investigators. They indicate that roentgen rays are not significantly phagicidal. Also they redirect attention to the rather widely accepted "target" theory which has been advanced to explain the phagicidal ineffectiveness of roentgen rays. The "target" theory assumes in essence that biological effects of roentgen rays are produced along "columns of ionization." These "columns of ionization". have a cross section (area) of from 0.72 to  $1.6 \times 10^{-10}$  cm<sup>2</sup>. In the theory this area is compared with the area (cross section) of a microbe or an ultramicroscopic particle. Phage particles (which are ultramicroscopic and of the order of 30 to 50 millimicrons in diameter) suspended in a liquid medium are small enough and far enough apart at a given level to permit "columns of ionization" to pass between them: to miss them, in other words. This concept is two dimensional whereas actually the field of experimental activity is three dimensional with time as a fourth dimension. In other words, the depth of the phage layer and the time of its exposure to the roentgen-ray bombardment are equally important with the areas of "columns of ionization" and of phage particles. Phage particles are electrically charged; also they should show brownian movement. Being very small they mutually repel each other. Consequently they tend to be disseminated uniformly in the suspending liquid. This repellent action is three dimensional. The combination of repelling force and brownian movement should preclude the probability of phage particles at different layers (each layer one particle deep) being in vertical alignment. Rather their distribution should be staggered; that is to say, particles at one level

(or layer) would tend to occupy interspaces between particles at higher and lower levels and so throughout the entire depth of liquid there would be a continuum of particles rather than columns of particles with vacant interspaces. Therefore, it would seem to follow that roentgen rays ("columns of ionization") should encounter more phage particles than spaces between particles in a layer 6 mm. deep. It will be recalled that the phages used in these experiments contained 100,000,000 particles per cubic centimeter. Yet after thirty minutes' exposure to roentgen rays (24,000 r) these phages, still or rotated, failed to show any significant inactivation. These experiments do not, of course, disprove the "target" theory. They do seem to indicate, however, that roentgen rays fail to inactivate bacteriophage within reasonable periods of time because they are inherently not phagicidal rather than that they fail to inactivate phage through poor marksmanship. These experiments are not to be construed as casting doubt upon the clinical value of the effectiveness of roentgen rays in treatment of disease within the body. Here the conditions are complicated and beneficial effects may be due in no small degree to stimulation or reinforcement of body defensive mechanisms (as liberation of enzymes from lymphocytes) remote from the foci of infection.5

#### REFERENCES

1. Beckwith, T. D., Olson, A. R., and Rose, E. J. Effect of x-ray upon bacteriophage and upon bacterial organism. *Proc. Soc. Exper. Biol. & Med.*, 1930, 27, 285–286.

2. Bruynoghe, R., and Mund, W. Action of radium on microbes. Compt. rend. Soc. de.

biol., 1925, 92, 211-213.

3. Colwell, C. A. Purified bacteriophage from lysogenic cultures, *Proc. Soc. Exper. Biol. & Med.*, 1937, 36, 100-103.

4. Crowther, J. A. Biological action of x-rays—theoretical review. *Brit. J. Radiol.*, 1938, 11, 132-145.

 DESJARBINS, A. U. Roentgen therapy for inflammatory conditions. Proc. Staff Meet., Mayo Clin., 1939, 14, 177-180.

 KAYE, G. W. C. X-Rays. Fourth edition. Longmans, Green & Co., Lond., 1923, p. 173.

 MIZUNO, K. Studies on effect of ultra-violet rays upon bacteriophage and its physicochemical nature, Jap. J. M. Sc. Tr., VI, Bact. & Parasitol., 1929, 1, 53-87.

8. Mohler, J. R., and Taylor, L. S. J. Research Nat. Eur. Standards, 1934, 13, 677.

Pugsley, A. T., Oddie, T. H., and Eddy, C. E. Action of x-rays on certain bacteria. Proc. Roy. Soc., London, Ser. B., 1935, 118, 276-298.

10. Schepmann, W., and Flecke, H. Extremely soft moentgen rays and bacteria. Klin. Wchnschr., 1926, 5, 1608–1611.

11. Spencer, R. R. Sensitivity, in vitro, of bacteria to beta and gamma rays of radium. *Pub. Health Rep.*, 1934, 49, 183–192.

12. WRIGHT, E. V., and KERSTEN, H. Effect of soft x-ray irradiation on bacteriophages. J. Bact., 1937, 34, 639-644.

13. WYCKOFF, R. W. G. Killing of colon bacilli by ultraviolet light. J. Gen. Physiol., 1932, 15, 351-361.



# CHEMICAL STRUCTURE AND ITS RELATION TO GROWTH AND DEVELOPMENT\*

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THIS is largely a statement of principles, such as is at times useful.

The healing art has two aspects—the immediate and the remote. The immediate is the relief of the sick. This is the function of the physician. The remote is the determination of the processes which underlie sickness. This is the function of the medical scientist.

The physician must perforce work from without inwards. From symptoms to their elimination. The medical scientist must work from within outwards. From the nature of being to its distortions and disturbances. It is necessary that the medical scientist be acquainted with the outer manifestations of the inner aberrations. It is useful for the physician to have insight into the possible inner bases of the symptoms he is attempting to alleviate. The acquisition of this insight is a long and laborious process. It depends upon the labor of the medical scientist and the clarity with which he can tell of his work and thoughts.

The present occasion is an attempt to set forth and to establish a point of view with respect to a natural phenomenon of general occurrence—namely growth. The subject is pertinent since no little attention is paid by roentgenology to tracing growth changes and to the correction of disturbances thereof.

Now it is obvious that progress in the study of growth, as of any process of nature, is more solid and more productive if the study is based on the four principal aspects of living things: direction, substance, state of substance, and form.<sup>1</sup>

Within the science of genetics is comprised the *direction* of growth, the determi-

nation of what course the development of living shall take. What substances shall be used not only to express the specific growth progression of any particular organism but also to compose the material thereof. What states these substances shall have for the activity of growth. And into what structural configurations they shall be combined in the production of the mature organism.

Within the science of chemistry is comprised the *substance* of living. The reaction basis of growth is founded in the chemical composition of its substance. No interpretation of any growth process is adequate until the nature of the chemical participants and determinants is known. No explanation can be finished until the responsible chemical reactions have been set forth.

Within the science of physics is comprised the *state of substance*. The state of substance is concerned with the rate and extent of growth activity. It is responsible for the reference frame of time. Such states as reside in permeability, imbibition, conduction, viscosity, the electrodynamic field, and cognate phenomena are sufficient examples of physical factors concerned in the acquisition and maintenance of that state of substance which is essential for growth.

Finally, within the science of anatomy is comprised that which deals with form. The form which substance takes in growing things. The shape, the arrangement, the juxtaposition, the connections, the extensions and the compressions of substance are the elements of anatomy. Within this science is comprised all that is concerned with architecture and structure; all that is concerned with space displacement and

<sup>\*</sup> Read in a Symposium on Growth at the Thirty-ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 20-23, 1938.

configuration as carriers of growth expression.

Thus, to recapitulate:

The direction of growth is the concern of genetics; the substance and expression of growth is the concern of chemistry; the state of growth substance is the concern of physics; and the form of growth is the concern of anatomy.

The immediate interest is with the substance or chemistry of growth and its relation to the several expressions thereof.

A definition of growth is indicated.

Now, growth is not single—it is multiple. It is the combined expression of developmental and incremental factors and processes.<sup>2</sup>

It is an lage formation as much as it is cell increase in number.

It is increase in cell specialization or differentiation as much as it is increase in cell size.

It is segregation of these cells into functioning tissues or organization as much as it is accumulation of mass of functionable substance or anabolism.

Indeed and in fact it is all of these—the summated expression of all those integrated processes which serve to produce the structurally and functionally mature organism.

If it be admitted that the reaction basis of growth is founded in the chemical composition of its substance; and if it be admitted that growth is not single but multiple, then it follows that each and every separate and specific growth process has its own particular set of chemical determinants, participants, and reactions.

No one would claim, I am sure, that the chemical processes concerned in cell division *per se* are the same as those which are responsible for the production of a bone cell from mesenchyma.

The participants of growth are of course the naturally occurring chemical constituents of tissues.

Knowledge of the chemical nature of the determinants of growth is increasing daily. One has but to glance at the multiplicity of

titles relating to the auxins—or stimulants of plant cell elongation—to realize that interest in the chemical conditioners of growth is today a very lively subject. Indeed, it is beginning to partake of the aspects of a bandwagon on which many an amateur mootler is climbing with unseemly haste.

With one possible exception—namely, that of the sulfhydrylsulfoxide equilibrium in proliferation—we know nothing of the immediate chemical reactions of growth.<sup>3</sup>

Now the properties—and hence the reactions—of chemical compounds are determined not only by their component atoms but also by the way in which these are arranged in the molecules. That is to say, in the domain of pure chemistry the structure is as important as the constituents. Therefore, since growth is an expression of reactions between chemical compounds; and since each growth activity has its own set of chemical determinants, participants, and reactions; and since differences between compounds resolve themselves into differences in structure as much as into differences in composition, it follows that any inquiry into the chemistry of growth must eventually resolve itself into an inquiry into the relation of chemical structure to growth and development.

A priori, then, the functions of chemical compounds in growth are conditioned by their structure.

The argument has now laid the foundation on which this topic can be developed.

Logic demands that the development be along three avenues of approach, namely, that of the participants, that of the determinants, and that of the reactions.

For purposes of simplification I will confine discussion to the components of the cellular proteins—the cytoplasmic and the nuclear. Fo the amino acids and the purine and pyrimidine components of nucleic acid.

These are chosen for three very important reasons. They comprise the bulk of living natter of all organisms. They provide the reaction basis for living, of which growth is a chief property. And they are

the naturally occurring chemical constituents of living tissue of general distribution.<sup>4</sup>

Concisely, they are the "Baustoffe" of growth wherever expressed.

Chemical structure is a significant factor with respect to the compounds used in tissue building.

It has been known almost from the beginning that the amino acids as they occur in nature have a definite configuration with respect to polarized light. Some turn it to the right and some turn it to the left. Strangely enough, many organisms seem to reject or to be unable to use the isomers of these naturally occurring compounds. To be utilizable the amino acids must have the same structural relationship to polarized light as those found in proteins.

Chemical structure thus determines the availability for growth of a large class of fundamental compounds.

Now the growth process which takes an entodermal cell and makes a liver cell out of it, and takes a mesenchymal cell and makes a muscle cell out of it is called "differentiation." The two kinds of cells are recognizably different in structural makeup even though both are built of amino acids. Analysis supports observation that the chemical structure of the protein molecule of the liver cell is distinct from that of the muscle cell.

Thus, differentiation is really a chemical specialization of the cell structure. Without this specialization there could be no distinction between cells; no differentiation phase of growth.

This difference lies in no small degree in the difference in proportion and arrangement of the constituent amino acids. In addition the chemical nature of the amino acid unions is most important to protein structure. 6.7 Indeed, it is possible that differences in these are real factors in establishing differences between many proteins.

Without doubt chemical structure is an influence in determining what the product of differentiation growth shall be.

Roentgen studies show that molecules tend to arrange themselves with regularity into a definite space lattice pattern which is characteristic for any given molecular type.

It is also a common property of molecules in combination to assume structural forms which are characteristic. Thus urease has one shape and hemoglobin another.

There is no reason to assume that the forces which determine these arrangements are abrogated when molecules are built up into living tissue.

It is, therefore, not impossible that the factors which contribute to definitive structural arrangements outside living tissue also contribute to the forms which living tissue takes as it is built of the characterizing molecules.

That is to say, the idea can be entertained that the structural nature of the
molecules which are used in tissue growth
may well condition the shape which the
growing part may take.

This morphogenesis is really expression of cell segregation which is called "organization" by the biologists. It is therefore possible that chemical structure conditions the product of organization as it does that of other growth activities.

These are but brief suggestions as to how the chemical structure of the building blocks of tissue is significant to growth through determining their availability and how through them it is significant in the production of differences in cell type and form.

Although the amino acids and other nitrogenous components of living tissue of general distribution function as building substance and energy, they also function as contributors of specific reaction properties to the protein molecules into which they are incorporated by the processes of growth.

But even more than this is the probability that each of these compounds plays a specific part in the regulation of some growth activity. The distinction here is between function as a component of tissue and function as a determinant of tissue; between the part played in providing the

reaction basis and the part played in activating and conditioning the expression of the reaction basis.4

An inquiry along this line has been going on at the Lankenau Institute for eleven years. As would be expected from the argument of the preceding paragraphs a relation between the chemical structure and the growth effect of these compounds has been traced in some instances. A few of these will be given to demonstrate the point.

In a growing organism part of the ingested food goes to produce new tissue and part to produce energy. When—other things being equal—energy expenditure increases, the amount of material used for growth is cut and mass increase is reduced.

Now it happens that the specific dynamic effect of glycine is less than that of alanine, and the specific dynamic effect of aspartic acid is less than that of glutamic acid. And alanine and glutamic acid differ from glvcine and aspartic acid by having one more CH<sub>2</sub> in the molecule. The indication is that the added CH2 is a determinant of the increased stimulation of energy expenditure by these particular compounds.<sup>8-11</sup>

Hence the chemical structure of glycine and aspartic acid in relation to alanine and glutamic acid is significant to growth in that the CH<sub>2</sub> difference influences the regulation of energy expenditure, which—in the growing organism—strongly factors the amount of material available for mass growth.

When an OH group is introduced into the molecule of some of these naturally occurring tissue components of general distribution quite an effect is produced.

Thus tyrosine is less toxic than phenylalanine and forwards differentiation.9

Hydroxyproline is less toxic, has less specific dynamic effect and forwards differentiation at lower concentrations than does proline.12,13

Serine is less toxic than alanine, has less specific dynamic effect, and may exhibit a special influence on differentiation. 9,14

Finally thymine, as compared with cyto-

sine, is less toxic and enhances differentiation to greater extent. 15,16

Thus, the introduction of the OH group into these four compounds acts to forward growth indirectly by reducing toxicity. It acts directly in the case of tyrosine, hydroxyproline, and thymine by conferring on them an added facilitation of differentiation.

Just because the OH compounds are better differentiation agents than the same compounds without the OH does not mean that OH as such is the differentiation effective agent. What is probably true is that the introduction of OH favors the formation of an effective configuration in intermediary metabolism.

Evidence suggests that this is pyrrolidone or some part or derivative thereof. This comes from the fact that a chemical relationship between the compounds which forward differentiation can be traced through this configuration.<sup>17</sup>

This brief exposition is sufficient to demonstrate the part played by chemical structure in the determinants of growth.

Turning now to the significance of chemical structure to the reactions of growth it is obvious that since the substance of growth is chemical and the processes of growth are expressions of reactions between chemical molecules or groups, the structure of these molecules and groups should be of particular importance.

Now it has been found that when a hydrogen of an amino acid such as alanine is replaced by a sulfhydryl, the compound may act as a stimulus to cell increase in number. The molecule may be single as cysteine or in combination with others as in the tripeptide glutathione.18

When it happens during the normal course of physiological oxidation activity that two such groupings unite with loss of hydrogen to form a disulfide in cystine-like union, the compound is no longer an active stimulant to cell multiplication.

And when this normal oxidation trend continues so that there is produced a compound in which the sulfur carries an oxygen

not only is there no stimulation of cell multiplication, there is even the opposite effect, a retardation of cell increase in number.<sup>3</sup>

Thus the chemical structure which develops during the normal course of living activity determines what the subsequent reactions shall be, which in turn determines what shall be the nature of the growth response. The change in chemical structure brought about by chemical reaction with the environment determines whether a basic type of growth expression shall be forwarded or held back; shall continue or shall cease to exist.

Although this principle has been demonstrated only with the sulfur groupings it cannot be doubted that all other growth activities are similarly conditioned. It must be so since the laws which govern chemical change in general must also govern the chemical changes of growth. And this principle is but the expression of the Second Law of Thermodynamics as extended to the Law of Mass Action. Which is in essence that the products of a chemical reaction tend to retard its further progress.

The foregoing paragraphs have given in all too brief survey the significance of chemical structure to growth and development. They have pointed out how structure is a sine qua non of the substance of growth; of the determinants of growth; and of the reactions of growth. If they stimulate intensive analysis of the substance of growth before and after its incorporation into living tissue in order that the nature of growth may be more accurately traced. they will have fulfilled their purpose. The stimulus can hardly have been delivered to a more appropriate spot since roentgenray analysis is the present basis of such information and roentgenology the science of its application.\*

#### REFERENCES

- 1. Hammett, F. S. Research institutes for biology. J. Heredity, 1938, 29, 255-257.
- 2. Hammett, F. S. The Nature of Growth. Science Press, Lancaster, Pa., 1936, 66 pp.
- 3. Hammett, F. S. Natural chemical equilibrium regulative of growth by increase in cell number. *Protoplasma*, 1930, 11, 382-411.
- 4. Hammett, F. S. Role of amino acids in developmental growth and its possible significance in cancer problem. Occasional Publications of the American Association for the Advancement of Science, No. 4. June, 1937, pp. 167–172.
- 5. MITCHELL, H. H., and HAMILTON, T. S. Biochemistry of the Amino Acids. Chemical Catalog Co., New York, 1929, 619 pp.
- 6. Wrinch, D. M. Pattern of proteins. *Proc. Roy.* Soc. Lond., 1937, A160, 59-86.
- BERGMAN, M. Structure of protein in relation to biological problems. Chem. Rev., 1938, 22, 423-435.
- 8. Hammett, F. S. Regeneration favoring effect of glycine. *Protoplasma*, 1936, 27, 65-68.
- 9. Hammett, F. S. Comparison of d-alanine, l-phenylalanine, and l-tyrosine with respect to their participation in developmental growth. *Protoplasma*, 1936, 27, 52-60.
- 10. Hammett, F. S., and Schlumberger, H. Role of l-aspartic acid in developmental growth. *Growth*, 1937, 1, 68-77.
- 11. Hammett, F. S. Differentiation forwarding activity of d-glutamic acid. *Protoplasma*, 1936, 27, 61-64.
- 12. HAMMETT, F. S. l-Hydroxyproline in developmental growth. Growth. 1037. L. 201-208.
- mental growth. Growth, 1937, 1, 291-298.

  13. Hammett, F.S., and Collings, W. D. Developmental growth and l-proline. Growth, 1937, 1, 285-290.
- 14. Hammett, F. S., and Rivard, D. Unpublished observations. To appear in *Growth*.
- 15. Hammett, F. S., and Lavine, T. F. Developmental growth and nucleic acid components. iv. Thymine. *Growth*, 1937, 1, 135-139.
- HAMMETT, F. S., LAVINE, T., and LAVINE, M. Developmental growth and nucleic acid components. v. Cytosine. Growth, 1937, 1, 189–193.
- 17. Hammett, F. S. Is the pyrrolidone configuration a specific chemical factor for differentiation? *Protoplasma*, 1938, 30.
- HAMMETT, F. S. Chemical stimulus essential for growth by increase in cell number. *Proto*plasma, 1929, 7, 297–322.



<sup>\*</sup> For discussion see page 279.

## RADIATION, MUTATION AND THE GENE\*

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GENES are the units of heredity. They occupy somewhat the same position in genetics as atoms do in chemistry. Genetic formulae are written with genes, chemical formulae with atoms.

Biologically speaking, genes are minute structures located in the nuclei of cells, normally in definite and linear arrangement on the thread-like bodies called chromosomes which condense into rods at cell division. Genes segregate and recombire in successive generations without losing their identity and exert a regulating influence on the developing individual so that it possesses the characteristics of its species or any hereditary variations from these characteristics derived from its ancestors.

Two complete sets of genes are present in all body cells (nerve, muscle or epithelium) and one set in the germ cells (egg or sperm). All body cells of a given individual are similar to each other in possessing the same set of genes derived from the fertilized egg. Each gene is named according to its most obvious effect but in reality each has many different effects, some structural, some functional. There is no evidence that any gene influences one trait alone. Every character, however simple, is dependent for its existence upon a number of genes. When the geneticist speaks of a gene for feeblemindedness he recognizes that even a feeble mind must result from the interaction of many genes all but one of which are genes for normality. The exceptional gene by which it differs from normal is the one designated as the gene for feeble-mindedness. It has been possible to study by genetic method only those genes which have nutated, leaving the great majority hypothetical.

Mutations or hereditary changes may be divided into two classes according to their effects: (1) "visibles," which change traits such as color, size, behavior, longevity, resistance to disease, structure of external or internal organs, and (2) lethals, which cause death of the individual at some stage in development. H. J. Muller in 1927 showed that roentgen ravs increased the occurrence both of visibles and of lethals up to two hundredfold. These induced mutations are similar to those occurring spontaneously. Definite desired mutations cannot be produced at will. We cannot aim at a single gene and cause it alone to mutate, but we can often select from the multitude of changes produced those that we desire to perpetuate and study.

Three types of chromosome and gene behavior may be listed as concerned with mutation: (1) loss or addition of whole chromosomes (radiation has played little or no part in this type of change); (2) rearrangements or losses of parts of chromosomes; (3) changes, probably chemical, within the gene itself.

Mutations of the second and third types are induced by irradiation. Those of the second type are considered in some detail as they have thrown much light on gene behavior and are highly important in radiation studies.

Representing by large letters the gense in two of the chromosomes derived from the mother and by small letters the corresponding or homologous genes from the father, the normal arrangement may be expressed as follows:

Irradiation may cause deletion or loss of a

<sup>\*</sup> Read in a Symposium on Growth at the Thirty-ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 20-23, 1938.

portion of one gene strand or inversion may occur as follows:

$$\begin{array}{ccc} A.B.C.D.E.F. & L.M.N.O.P.\mathfrak{Q}. \\ \text{Deletion} & \text{Inversion} \\ & a.f & l.p.o.n.m.q. \end{array}$$

A portion of one chromosome may be translocated to a non-homologous chromosome and this is usually a reciprocal exchange.

$$A.B.C.D.E.F.$$
  $a.b.c.d.N.O.P.Q.$   $l.m.n.o.p.q.$ 

Changes of these various types result in very irregular distribution of hereditary material in the formation of the germ cells, and the fertilized eggs may fail to develop or may develop into weak or abnormal and genetically unbalanced mutant types in whose descendants the condition continues.

It was formerly thought that genes functioned independently of their arrangement in the chromosomes, that no difference would be caused by rearrangement provided that the same set of genes was present. It now appears that certain genes undergo a "position effect" when they are brought into a new arrangement in the chromosomes. Thus as a result of inversion the gene E may be brought close to gene A. A then has a "position effect" on E changing it to E' so that its influence on a certain trait is modified. The chemical

$$A.B.C.D.E.F.$$
  $A.E'.D.C.B.F.$ 

interactions appear to change with change in position. This is a type of mutation. When the modified gene is returned to its former environment it returns to its old behavior, a reversionary mutation. The influence, then, of new gene neighbors is temporary.

In addition to the above-mentioned gross chromosomal irregularities, there may be deletions of single genes, A.B.D.E.F., or minute inversions, A.B.D.C.E.F., or additions by translocation of one or two genes only, A.B.C.N.D.E.F., so that some have thought that all mutations are rearrangements of chromosomal materials. The

majority of geneticists, however, still appear to favor the view that chemical changes within the gene, mutations in the narrow sense, likewise occur.

Until very recently students of the physical basis of heredity were dependent for their cellular material on the minute chromosomes as seen in dividing cells, but since the discovery by Painter in 1933 of the significance of the giant salivary gland chromosomes of Drosophila, two hundred times as large as those previously studied, it has been possible to see the minute location of the genes if not the genes themselves. These chromosomes appear as cross-banded cables made up of chromatin fibers, the bands being formed by minute granules (genes?) on the fibers. Each cable .. is double (derived from a fused pair of homologous chromosomes) with homologous bands of granules apposed so that it becomes relatively easy to see if any of the bands in one of the homologous (parental) chromosomes are missing or displaced. Thus chromosomal abnormalities may be minutely and directly observed.

What can be said of the nature of the gene itself? Estimating from genetic data the number of genes in the sperm or egg of Drosophila to be about 2,000, Morgan, Bridges and Sturtevant in 1925 supposed the diameter to be from 2 to  $6 \times 10^{-2}$  micra or slightly larger than a molecule of hemoglobin. More recent studies, based on mutation rate under the influence of radiation and also on observation of bands in salivary chromosomes, estimate the number in egg or sperm of Drosophila, to be 5,000 to 15,000, the size from  $2.5 \times 10^{-3}$  to  $1 \times 10^{-14}$ micra and the structure that of a single large protein molecule over five times as long as thick, or of several (15?) protein molecules.

As regards different kinds of genes, Gowen and Gay (1933) from mutation rate in roentgen studies of *Drosophila* divide genes into dominant vitals, 52.7 per cent; recessive vitals, 39.5 per cent; dominant visibles, 0.6 per cent; recessive visibles, 7.2 per cent. This statistical analysis does

not tell us whether the vital factors might produce visible changes if they varied in some other way or whether the genes giving visible changes are necessary to the life of the organism.

Some genes are of the eversporting variety, mutating very frequently while others are known to have changed but once. Some have mutated several times in the same way while others have mutated in a great variety of ways. One gene for eye color in Drosophila has undergone at least ten changes from wild type giving different colors and there are two different wild type forms of this gene known which differ only in their direction and rate of mutability. Some genes are known to take dozens and •probably hundreds of different forms, as one for bristle distribution and number in Drosophila and one for kernel coat color in corn. However frequently changes may occur they are discontinuous, like changes in chemical molecules, rather than continuous like variations in a mass of material. In comparing changes in genes with chemical reactions it is to be noted that we deal not with a mass of independently changing molecules in a test tube, but with a mass of descendants of a single changed molecule. descendants through a succession of autocatalytic reproductions corresponding in number to the number of cell divisions necessary to form the individual or the succession of individuals.

Radiations produce mutations, probably because they can get directly at the germ plasm without too great injury to the protoplasm in general. Within the roentgenray range, wave length seems to make no difference, nor is intensity during treatment an effective factor. Total dosage is what counts and mutation rate increases with increasing dosage on the average in a straight line logarithmic curve. If, however, gross chromosomal abnormalities are separated from very localized or single gene changes, the frequency curve for the former tends to slope down with increasing dosage relative to that of the latter which slopes up. It appears that changes in single genes

are caused by single hits while two hits are necessary for translocations or inversions, hence the difference in the type of curve. If mutation rate is low, as when dosage is low or in spontaneous changes, the chance of two breaks occurring at the same time in the chromatic threads of one cell is very slight. A single broken thread will unite again where it was hit and so there is a localized change only, and there will be practically no chance for union of two different threads.

Dosages of 2,000 to 5,000 r are convenient for producing mutations. After 10,000 r there is a dominant lethal change of some sort produced in practically every sperm cell. Dosage for egg cells must be much higher for the chromosomes are not so closely packed together and apparently the closer the packing the better the chance for irregular recombinations. Dry seeds stand a much higher dosage than sprouting seeds with cells undergoing divisions but since lethal changes are relatively low in the former, it is better to use the more resistant material in order to obtain a maximum of viable visible changes.

Ultraviolet radiation is effective in causing mutations but there is here the difficulty of getting the rays into the germ plasm without too much superficial injury. Pollen cells in a single layer can be conveniently treated and ultraviolet radiation has a different effect than roentgen rays, causing no increase in translocations, but producing many single point mutations. A further difference is that ultraviolet radiation applied to pollen produces breaks which are transmitted to only half of the resulting cells while, with roentgen rays similarly applied, all the subsequent cells are affected. It is as if the chromatin thread were already beginning to split and the roentgen rays affected both daughter strands while the ultraviolet radiation affected only one.

Neutrons have been shown to be highly effective in producing mutations. The work here is just beginning but it has already been demonstrated that the effect increases with increasing dosage and that the influence is much more potent than that of roentgen rays if comparison be made in term of roentgens. The radiation is a mixture of gamma rays and fast neutrons and is not properly defined in roentgens. To avoid confusion the units as indicated by the r-meter have been termed pseudoroentgens.

Short radio waves such as used in thermotherapy, and ultra-short waves have had no influence on mutation rate although they were applied in intensity high enough to kill most of the insects used.

Temperature differences at which the cultures have been reared change mutation rate and this according to van't Hoff's rule.

The coefficient of change for 10° C. (Q<sub>10</sub>) is about five, much higher than the ordinary values for a chemical change, between two and three. This follows because the rate of reaction of a single gene is very low, of the order of one change in one thousand to several hundreds of thousands of generations, very much lower than the rate for chemical reactions as observed in the laboratory.

Finally, various chemicals have been used in attempts to affect genes but results have been negative, probably because the chemicals cannot get at the genes without killing the protoplasm.\*

\* For discussion see page 279.



## THE BIOLOGY OF THE CANCER CELL\*

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WHICH of the many processes commonly grouped under the term "growth" produce that growth which is called "cancer"? And wherein does it, or do they differ from the corresponding phases of normal growth? The answers to these questions couched in biological terms must be the points of departure for discussion of the biology of the cancer cell. From then on various radiating leads may be followed to see where they go, but always in terms of comparison with normal cells.

Arbitrarily, we may divide certain phases of growth into the processes of initiation, multiplication, differentiation and organization. Because of lack of time, this presentation must be confined to a brief comparison of them in normal and cancer protoplasm.

Cancer cells do not organize into definite structures, and this is the basis of our means of diagnosis. If they did organize, then a woman with cancer of the breast, instead of harboring a mass of cells which grow on and on in any and all directions and into no constant shape or structure, would develop another breast; a patient with carcinoma of the rectum, another rectum, and so on. At least another definite structure would be produced if cancer cells organized. Therefore, lack of organization must be compared to presence of organization as displayed by normal cells. But this is the very problem which is now rapidly coming to the fore in all of biology. In my opinion it is the core of biology. Why is it that the offspring of dogs are always dogs; of sea urchins, sea urchins; why do human mothers always produce some sort of sample of Homo sapiens? Why are livers shaped as they are; how is it that a giraffe's front leg is so built that it can be distinguished from a human arm by even the

inexperienced in anatomy? And another most important question is, how is differential growth maintained, which means that in a given organism liver is not too large for heart which is not too small for kidneys, etc.? One of the most dramatic of all biological occurrences is that growth in all the meanings of this word takes place in relation to a Whole; all of the complicated processes head toward the completion and maintenance of a thoroughly integrated organism. This is organization. Its orderly progressions may be used as a starting point for the construction of a whole system of synthesis of knowledge and thought. i.e., a philosophy, something which is needed very badly at present. I risk the objections and even scorn of many by emphasizing this. Even some scientists are afraid of thinking, let alone speculating constructively to guide them in their experiments and application. But this is not the time for further development of this theme.

If, then, normal cells organize, it is obvious that the cells must be there to accomplish this. They get there by multiplication. And further, they differentiate into different kinds of cells before they organize. Thus:

- 1. Cells organize when they have multiplied and differentiated.
- 2. Cells differentiate when they have multiplied.
  - 3. Cells multiply.

This is but a restatement of the well known autonomy of cells and their capacity to grow; the seedling splits the granite rock in which it embeds itself. From which it may well be that:

a. Cells multiply in order to differentiate and organize.

<sup>\*</sup> Read in a Symposium on Growth at the Thirty-ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 20-23, 1938.

- b. Cells differentiate because they have multiplied and in order to organize.
- c. Cells organize because they have differentiated and multiplied.

This method of statement has a teleological flavor, but what of it if it leads to further useful concepts such as:

- x. Cells cease multiplying because they have differentiated and organized.
- y. Cells cease differentiating because they have organized.

It follows then that:

z. The natural inhibitors of cell multiplication are differentiation and organization, especially the latter.

Cancer cells continue multiplying, else they would not plague us as they do. They differentiate poorly and as stated, they do not organize at all. Can it be then that cancer cells continue multiplying because they do not differentiate properly and do not organize at all? If so, do they fail to organize because they cannot, or because the environment does not give them the proper building blocks to utilize for this function?

These two questions to me are fascinating, and I have not hesitated to adopt provisional answers as one of several central themes for the construction of plans for experiment. Indeed, I have used it as the basis of a definition of cancer to give force, direction and logic, not only to further exploration, but also to practical everyday experiences in the handling of cancer patients.

I believe, at present, that cancer cells do not organize because they cannot, and this is the reason they continue multiplying.

Since most organisms, including humans, are composed of protoplasm which has differentiated into cells, I will lay the emphasis on cellular terms, even though the old cellular doctrine has lost its force as a generality and become a special case, not only anatomically but also physiologically. For from the anatomic point of view, there are many large, perfectly competent organisms consisting of only one cell, and physiologically it may be said that one of

the differentiations which protoplasm can undergo is that of dividing itself into cells. Even in human development, some tissues begin as syncytia and now and again a human tumor is encountered containing nuclei but no cell walls, i.e., a tumor as a syncytium. Thus the biology of tumor protoplasm must also consider the biology of plasmodia. Interesting though this is, again we must forego for a future session. Finally, it may be remarked that Mrs. Harvey, by centrifuging sea urchin eggs and removing their nuclei, has nevertheless observed cell division up to 500 or more cells and some differentiation without any nuclei at all. I have never encountered a tumor with no nuclei, but a normal analogy might be cited in the blue-green algae' which have cell walls but no nuclei. Not even chromatin has been detected with certainty and yet they breed true; i.e., they differentiate and organize. All this is recited not so much to show how complicated the organization problem is, but to call attention to the fact that material for cancer study and comparison lies on every hand.

#### CELL MULTIPLICATION

The multiplication of cells means their increase in number; a single center of protoplasmic activity becomes two. Both normal and cancer cells multiply. Many studies are recorded in which the anatomic processes of division have been studied and the results have been nothing characteristic in the division process of malignancy.

In tissue culture the rate of division of cancer cells is at least as rapid and probably more so than in rapidly growing normal cells, e.g., connective tissue. In the animal body, cancer cells do not multiply as rapidly as normal cells can. This statement is usually challenged out of an old habit, but when it is remembered how quickly granulation tissue can grow, or how quickly a portion of liver may regenerate, we become thankful that a malignant growth does not reach the size of a human kidney in ten days or two weeks. And yet a liver can regenerate that rapidly.

Nor does increasing the rate of multiplication of normal cells lead to malignancy. When a normal chemical stimulus to division is used, e.g., sulfhydryl, there result more rapid differentiation and organization of the cells, but into normal parts or into "bigger and better" parts or whole organisms. Nor does altering timing relations lead to malignant growth. As an organism or a part is developing, or as regeneration, etc., takes place, the cells in the mass of living protoplasm are in different stages. some just multiplying, others differentiating, others organizing in the exquisitely timed sequence necessary for a perfectly formed structure to result. It is possible to interfere with this timing by, e.g., acceler-• 'ating or retarding the multiplication phase, but no malignancy results. A misshapen part or at most a teratological structure results, but it organizes and stops growing.

Finally, it must be emphasized that cell cleavage *per se* is not the cause of differences between cells or tissues; it is not even always the first step in development, nor is it a factor in determining the kind of differentiation which a cell undergoes.

I do not think, therefore, that malignant growth is fundamentally a disease of cell division.

#### DIFFERENTIATION

When a cell differentiates it is transformed from the more general to the more specific. It turns into a unit capable of functioning as a part which helps maintain the organism as a Whole. In passing from an undifferentiated to a differentiated state its chemical composition is rearranged, a mesenchymal cell may become liver or bone; we no longer recognize the sacredness of the three germ layers. Many times definite and specific combinations are built to manufacture certain definite substances; thus, thyroxin in thyroid cells, saliva in salivary cells, and so on. Differentiation is always accompanied by organization, i.e., numbers of differentiated cells are gathered together in definite form to make a structure like a thyroid gland, salivary gland, etc.

The ability of a cell to differentiate, i.e., turn in so something, is called its potency. An interesting and important question is how much of this potency of undifferentiated cells resides within the cell and how much is impressed upon it from without, i.e., from its environment. Again, there is no time to marshal evidence on this question and so we must be content merely to summarize. A large part of the potency which a cell can display is inherent within it, i.e., it is inherited as a part of the lineage from which it came. Certainly, species specificaty is inherent, for embryo sea urchins and starfish develop into their respective animals even when living in the same er vironment.

A most important property of undifferentiated cells is that their potency is greater, both qualitatively and quantitatively, han is normally expressed. Thus, e.g., if the two cells of a divided sea urchin's ovum are separated, each will develop a perfectle competent new sea urchin. If this process is repeated, as many as eight sea urchins can develop from one ovum. The potency ordinarily displayed by a sea urchin's egg is one sea urchin, but it can give rise to at least eight. Its potency, therefore, is greater quantitatively than its normal realization.

There is one layer of living cells between the bark and wood of a tree, say, even one of the gant sequoias. Every now and then one of these cells divides; one daughter cell stays put, i.e., remains undifferentiated as what I call a "spare part" for future dividing. The other differentiates into either wood or bark as the occasion demands. This is an example of excess potency of the qualitative kind. Which of the potencies and how much a cell uses is determined by its environment in the broad sense of the word.

Another important consideration about differentiation is that a completely differentiated cell can no longer divide. There are, of course, stages to differentiation which are very difficult to measure, in fact have no been measured quantitatively as

vet, because of the inherent difficulties of the problem. It cannot be said, therefore, at what stage in differentiation a cell loses its ability to divide. We do not know of how much or what kinds of differentiation protoplasm is really capable; if we did, it would be possible to predict the future course of evolution more accurately than the wild guesses in which some indulge. Perhaps, however, it is when a cell enters into the last phase of differentiation, which it will undergo in the organism of which it is a part, that it loses its ability to divide. Differentiation, then, is the natural inhibitor of multiplication as stated in the preliminary remarks.

Finally, when a cell is differentiated, I believe on indirect but nevertheless good grounds without being able to bring certain proof, that it cannot retrace its steps and become undifferentiated again. A tissue can be de-differentiated in the sense of a more specific tissue being replaced with a less specific one—yes, but the replacement is not by the previously differentiated cells which de-differentiate. These cells perish and are replaced by new ones coming from undifferentiated cells—spare parts—which do not differentiate as far quantitatively, or the same qualitatively, as the tissue destroyed.

Granting, then, these two propositions and, as stated, there is proof of the former and I believe good evidence of the latter, viz., that (a) the potency of a cell is greater than its normal realization and (b) it cannot de-differentiate, a number of conclusions emerge in relation to malignancy. Among them are these:

Malignant growths arise from incompletely differentiated cells, i.e., "spare parts."

These "spare parts" are, of course, essential to survival of any organism, for from them come the cells to replace those worn out, e.g., the skin, blood cells; for physiological hyperplasias, for repair. Normally to repair a wound, cells multiply, differentiate and organize until repair is completed, i.e., organization is restored. If

these "spare parts" multiply but do not differentiate properly and do not organize at all, we encounter what we call malignancy. If then potency is greater than realization, as it is, there should appear in malignancy many different pictures corresponding to no organization and perverted differentiation. This is exactly what we see and one of the horrors of it is the number of different names given to tumors and still being coined to the utter confusion of pathologist, roentgenologist and clinician alike. The essentials are: malignant growths arise from division—capable, therefore, incompletely differentiated cells, i.e., "spare parts," which having excess potency but not differentiating normally turn into pictures of infinite variety. We have dignified. these varieties by separate names as though they were entities.

Of assistance in this naming process is the fact that there are degrees to the loss of differentiating ability displayed from tumor to tumor. This important fact has practical application. As a rule, tumors with less differentiated cells are more easily controlled by irradiation, but they grow more rapidly because they contain more cells of low differentiation which have not lost their power of division.

As stated, I believe at present that the reason cancer cells do not differentiate properly and do not organize at all is because they cannot. It will be impossible to consider all the reasons for this statement for it would require a considerable text on organization alone. One fact, however, may be mentioned. It is a common experience to see both normal and cancer cells multiplying in the very same environment, the former differentiating properly and attempting to organize, the latter not. Apparently the same building blocks are offered to both, but the cancer cells cannot use them. Some change has taken place inside of them. Since this change is transmitted from mother to daughter cells in much the same way and degree as the cancer grows, it is spoken of as "somatic mutation." Unfortunately, the word mutation is

subject to a variety of meanings and imputations. In the present connection my personal definition is "a transmissible, irreversible change in the composition of the cell involving its potencies of differentiation and organization." Lewis says the cancer cell is a new race of cells, which is about the same thing.

Numbers of different wavs have been found to produce cancer experimentally. Among a long list of chemicals are tar, dibenzanthracene, methyl cholanthrene. To date, no one group or combination of atoms has been found to unite and correlate these.

Certain viruses produce cancer. So do roentgen rays. An important question still unsolved is whether cancer can be produced by any method in an animal which is not genetically predisposed. Certainly, guinea pigs are resistant; we have rubbed the skins of a number of guinea pigs three times a week with dibenzanthracene for five years until they died of old age without cancer appearing. On the other hand, certain strains of mice can be bred with less resistance to carcinogens. But these questions can be discussed no further.

In seeking a generalization it is at once apparent that lack of organization is a common factor in all malignant growths. Introducing some of the above considerations we may state provisionally and as a basis for exploration that a cell becomes cancerous when it loses its ability to pick up the requisite building blocks from the environment and build them up into the proper chemical composition and physical arrangement which responds to surrounding fields of influence and organismal forces. Words, and more words! yes, but chemical carcinogens, viruses, roentgen rays, chronic irritations produce cancer by changing the chemical and physical composition of division—capable cells. What are the chemical compositions of cells; what changes are undergone when a cell differentiates; what chemicals influence growth and develop-3 ment and what phase? I could go on indefment and what phase? I could go on indef-thenigh tumers; others are malignant. There is initely and ask questions which can be one point, for example, in the sex chromosome

made subject to experimental attack, and that is the important fact of this discussion.

#### DEFINITION OF CANCER

Cancer is a mass of cells that arise from and continue to proliferate within an organism as a result of and in direct proportion to the extent of their internal qualitative differences from the other cells of the organism particularly with respect to the potencies of differentiation and organization.

#### DISCUSSION OF PAPERS BY DRS. HAMMETT, WHITING AND REIMANN

DE. STANLEY P. REIMANN, Philadelphia. I do not want to say very much in discussion of these papers. I simply want to thank you for the opportunity of bringing a little bit of biological lore to your meeting because I feel, as you do, that the basis of our profession is biology and that if we know more biology we will be better doctors; that if we do anything in medicine which is contrary to the proper principles in biclogy, we are not practicing proper medicine. Therefore, I, for one, am very glad to bring these few random thoughts on the biological undermeath of some of the things which perplex as in this particular growth problem of malignant disease; not that these things do not perplex us in normal growth too, for they do, but they are particularly perplexing in malignancy. I can see nothing better as an approach than to start from the biological side, whether from olans, from animals, from high or lowly organisms and then add to it as much chemistry as possible and as much physics as we can.

DR WHETING (closing). It seems to me that these various phases of the problem of malignancy come together very nicely. Dr. Reimann mentioned fundamental changes, internal changes in malignant growth, and it seems to me that those are really somatic mutations. Perhaps they are not, but we do not know enough about the chromosomes in cancer cells in matignant growth. We have in the fruit fly, Drosophita, a number of definite genetic factors which cause malignant disease and various tumers, and we know at what point, in what chromosome, these various factors are located. Some of the tumors developed are so-called which causes a benign tumor. A tumor develops in the body cavity of the larva and sometimes it kills the animal, sometimes it does not, but it is usually benign because it happens to occur in certain places that are not vital; the animal does not die. It can go ahead and reproduce. That is a very definite change, a mutation in a very definite gene located at a definite point in the sex chromosome which causes this.

I have said that all of the cells of the body are of the same genetic constitution in the fruit fly. There are, however, certain exceptions. I believe that the tumor cells in the affected flies have changed; that is, something happened to a gene or chromosome so that it mutates. It has become unstabilized and therefore it can change at some point in development, and that point varies apparently according to chance. In the same stock, we get different conditions.

To come back to the matter of viruses, the viruses are said by some to be free genes, floating around loose. There is a good deal of evidence that there may be something to this idea, because of their rate of mutation or their rate of change under treatment with roentgen rays and so on; also, the size of the virus molecule, whatever that may be, is similar.

It seems to me, therefore, that a great many of these points are really coming together, the study of radiation effects and somatic mutations—of course, we do have somatic mutations; I showed some in my slides, where a certain portion of the chromosomes was knocked out by irradiation; that is, certain cells produced white eyes in a red-eyed fly, because white was recessive there. That is also true for bristles there. We have all sorts of changes that may be brought about in the body by treatment with radiation.

Of course, those are not cases of malignant growth but other cases may be; we may produce malignant growth by irradiation or we may knock it out so that the cells which would go ahead and multiply or proliferate are not able to do so because they have what a geneticist would call dominant lethal conditions, the same sort of thing or very similar to the thing we are able to produce in the sperm cell, so that the egg which is fertilized is thereby killed; an egg which would normally develop parthenogenetically. Other forms do not develop parthenogenetically. We cannot get any statistical evidence on these because we do not know whether or not the egg is fertilized. Here you

know that it is fertilized if it dies; if it is not fertilized, then it does not die.

Dr. Rollin H. Stevens, Detroit. This discussion has been very stimulating. I may be getting to be rather an old man now because in my spare hours I have been trying to learn something about these "spare parts" and newer developments in different branches of science that enter into our knowledge of disease, particularly of carcinoma. We must keep abreast of the natural sciences. We should have much more of them in our future programs. It might be a good idea to have some of these essayists on the lecture series such as we have been having in the mornings, for it seems to me this newer knowledge is fundamental to our understanding of cancer.

I would like to offer a motion that we extend a vote of thanks to the gentlemen who have taken part in this program this afternoon. I think it has been a very fine part of our meeting here.

Dr. Alexander H. Pirie, Montreal, Canada. I would like to second that motion, and also to comment upon how this extremely scientific work is being used commercially. I little thought that my gardening, of which I am so fond, would come up in a meeting such as this. I have been using indolacetic acid to make my plants grow. I never thought I would hear about it here today. But it is becoming commercial, and I have seen some cuttings grow in a way that I never expected by using this acid, which I heard mentioned today by one of the speakers.

Dr. E. P. Pendergrass, Philadelphia. I would like to ask Dr. Reimann if, in closing the discussion, he would comment upon colchicine and whether that has any value as a therapeutic agent along with irradiation.

Dr. Reimann (closing). I was amazed when I first saw what colchicine does. It was shown to me by Dr. Ludford in England. All the cells stopped proliferating in a certain phase of multiplication and there they were, a perfectly gorgeous picture of mitosis.

Therefore, if the roentgen rays hit cells harder while they are in mitosis, it appears theoretically to be a good drug to give before roentgen treatment, because then there would be a great many more cells—division-capable cells, of course, for if they are not division-capable, they won't go into mitosis—there would be a great many more division-capable cells in mitosis at

a certain time. Then the dose of roentgen rays could be delivered. At what time? Well, experiments with mice—and note that they were not transplanted but spontaneous tumors—an important distinction, in spontaneous tumors of mice the maximum effect is found about four hours after colchicine is given to them in comparatively large doses.

We happened to be doing some biopsies and we gave some patients colchicine at different times before the piece of tissue was taken out. We dropped the tissue in the appropriate fixative and stained it in the appropriate way. We found, sure enough, that in a few patients it was possible to arrest many of the cells in mitosis at this particular phase. That was about four hours after the dose was given.

Unfortunately, in order to give a sufficient dose to stop every cell in mitosis, it is necessary to give too much colchicine for the comfort of the patient. On the other hand, we have given as high as 1/60 of a grain by mouth, and four hours later we have taken a piece of tissue, and many of the cells in mitosis were arrested in that particular phase. On the basis of that, I believe some roentgenologists have given colchicine and then delivered their roentgen-ray dosage.

It will take a long while, of course, to tell whether delivering it that way is better than delivering the dosage to the same kind of tumor without colchicine. Unfortunately, you cannot tell what would have happened if you had not given the crug. This is one of the fundamental difficulties with which medical men are always confronted. However, dosages as high as 1/60 of a grain can be given, and if it helps just a little bit to destroy some cells, certainly it is worth while using and trying, at least from the theoretical point of view.

The colonicine loses its effect after a period of ten to twelve hours in mice. I do not know how long it beeps its effect in humans because we have not pursued that to the extent of being able to say anything definite, but it keeps the cells there for a period of a number of hours at least beginning about four hours after the dose is given. Then, after a while, when it lets go, the cells go on and multiply; the tumor keeps right on growing.

What happens to human tumors in respect to doubling caromosomes from colchicine and all the rest of that, I do not know. I sometimes get pieces of timor and fix them in Flemming's solution or others and ask my friends, the cytolog sts, to look at the human chromosomes. They always look at me dismally and say, "That's an awful job, to look at human chromosomes," so I don't get very far with that. Maybe that is one of the reasons why I can't answer a few very definite questions which you may have in mind in relation to colchicine, questions which we ought to be able to answer but just earnot do so as yet.



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Twenty-fifth Annual Meeting: New York City, June 10-11, 1940.

## ≈ E D I T O R I A L S ≈

### TREATMENT OF OSTEOGENIC SARCOMA

OSTEOGENIC sarcoma is a dread disease and its treatment is fraught with considerable disappointment. Amputation is the treatment commonly urged for osteogenic sarcoma of an extremity and it has always been believed that the earlier the amputation was done the more hopeful would be the outcome of the case.

Recently Ferguson\* has reviewed the first 400 cases of osteogenic sarcoma in the Registry of Bone Sarcoma of the American College of Surgeons, excluding those cases with inadequate data or where the diagnosis was seriously disputed. From an analysis of this group of cases he draws the conclusion that early amputation not only is not the best treatment but it actually tends to assure the death of the patient. "Early amputation" is interpreted by Ferguson as amputation within six months of the onset of symptoms.

In his analysis he classified survivors as patients living with no evidence of tumor at the last report more than five years after amputation and the last surgical treatment.

It is interesting to note that only 8 per cent survived early amputation, whereas 29 per cent survived later amputation. This survival difference, Ferguson says, cannot be explained by a lesser degree of inherent malignancy in patients having delayed amputation. This is evidenced by the fact that in patients in whom one or more pathologists thought that histological study indicated a lesser degree of malignancy 14 per cent survived early amputation, whereas 41 per cent survived when amputation was delayed. Singularly enough, early amputation was fatal even when malignancy may not have been great.

In another group of cases in whom one

or more pathologists thought that the lesion might be of unusually high malignamcy, only 4 per cent survived early amputation and 37 per cent survived when amputation was delayed.

In a given lesion of the extremity one might think that early amputation would be the proper treatment for osteogenic sarcoma and that the earlier the amputation, the better would be the results. Contrary to this, however, Ferguson found that amputations which were performed within the first six months after the onset of symptoms yielded the poorest results. In those patients where the extremity was amputated in the first month after the onset of symptoms none of the thirteen patients survivee. With amputation in the second month one of twenty-five patients survived; with amputation performed in the third month, two of twenty-three patients survived and where the amputations were performed in the fourth, fifth and sixth months following the onset of symptoms eight of seventy-three patients survived.

In the face of such an analysis one can only draw the conclusion that "very early amountation is fatal."

A further study of the history of the patients brought forth the information that of the eleven patients that survived early amputation all were in the age period of from eleven to twenty, and all but one had lesions at the distal portion of the femur. Ferguson remarks that in this series a patient had practically no chance of survival following early amputation unless he was in the age period of from eleven to twenty and unless the disease was located in the distal portion of the femur.

It is the practice of some institutions to administer irradiation before amputation. Fergusor's study of this group of cases indi-

<sup>\*</sup> Ferguson, A. B. Treatment of osteogenic sarcoma. J. Bone & Joint Surg., Jan., 1940, 22, 92–96.

cated that irradiation before amputation seemed to improve the results of early amputation but did not definitely affect the results of late amputation, and he also elicited the information that irradiation alone did not effect a cure in any case in this series of 400 cases. He did find, however, that excision before amputation appeared to be a useful treatment as his study showed that when excision preceded amputation 17 per cent survived early amputation and 29 per cent survived late amputation.

The results of early amputation and those of late amputation were not notably affected by any treatment except excision or irradiation before amputation nor were they notably affected by such incidents as biopsy, fracture, or incision and drainage.

If the results from early amputation are so poor, what method of treatment could be instituted to bring about better endresults? Frankly, Ferguson, says that if early amputation is wrong, the best way to treat the early case of osteogenic sarcoma of an extremity is at present unknown. But the results might be improved, he says, by delay of amputation, with irradiation during the period of delay, which should further improve the end-results, and excision might be used to advantage before amputation.

Exactly why delayed amputation offers a longer period of survival or cure is not quite clear. Ferguson advances a theory that in the early months of osteogenic sarcoma the growth is a rapid one and the disease does not consist solely of a local lesion but of a local lesion plus innumerable tumor cells circulating in the flowing blood. These free tumor cells apparently need some aid to enable them to leave the blood stream and locate where they grow. The shock attendant upon the amputation produces this aid in the migration of the tumor cells, but for some unknown reason minor operations such as biopsy, incision, curettage or excision do not offer the same aid. He therefore suggests that the time selected for amputation be done in a quiet period. This quiet period could be determined by the fact that there had been no sudden increase of pain or of size of the tumor for at least two months and that there was no recent weight loss and when the roentgenogram revealed no evidence of extension of the tumor or increase in the size of the soft tissue mass.

Immunity or resistance to the tumor is discussed and Ferguson refutes the idea that the better results of late amputation are due to this as exemplified by the results of excisions. It was found that early excisions yielded much better results than those performed more than six months after the onset of symptoms.

It is apparent that the proper treatment of osteogenic sarcoma of an extremity should be to find or to create a proper time for amputation and then to amputate. . What are the factors that tend to create a proper time for amputation? Irradiation is useful, he says, in that it tends to reduce the more virile cells to a less virile state in which they are less apt to be able to form metastases in the lungs at the time of amputation. Excision is also useful. It was also found that when bone grafts were inserted at the site of excision of osteogenic sarcoma the development of recurrence was retarded, the bone grafts or chips filling in the space which otherwise would be occupied by blood clot or fibrin, media suitable for the growth of tumor cells.

The treatment which Ferguson advocates for osteogenic sarcoma of an extremity as a result of his analysis of the large group of cases is: (1) avoidance of early amputation; (2) delay of amputation; (3) irradiation before amputation; (4) irradiation, excision, and implantation of a bone graft or bone chips before amputation, with amputation following before recurrence becomes evident; (5) repetition of excision before amputation, if recurrence is evident before amputation has been done.

It can readily be seen from this analysis that the present treatment of osteogenic sarcoma is far from ideal and possibly as a result of this careful study a better or more universal form of therapy may be evolved in the treatment of what is now a rather hopeless condition.

## GLENN R. FORD 1893–1939

DR. GLENN R. FORD of Endicott, N. Y., was born on July 1, 1893, at Cazenova, N. Y., and died on September 9, 1939. He was a graduate of the Fulton, N. Y., High School, and of Syracuse University in 1919. He interned at the Rochester General Hospital, and spent a year in the post-graduate study of radiology at the University of Pennsylvania in 1921–1922. He was engaged in private practice in Rochester, N. Y., in 1922 and 1923, and entered the Endicott Johnson Medical Service on March 15, 1923. He was a member of the Binghamton Academy of Medicine; Broome County Medical Society; Central New York X-ray Society; also a diplomate of the American Board of Radiology, and became a Fellow of the American College of Radiology, in 1939. He was also elected to membership in the American Roentgen Ray Society in 1939. Dr. Ford was in charge of the Department of Radiology at Ideal Hospital, Endicott, N. Y., and also at the Charles S. Wilson Memorial Hospital, Johnson City, N. Y. He was married, and is survived by his wife and one child.

#### RESOLUTIONS

Whereas On September 9, 1939 death un-

duly claimed our respected colleague, Dr. Glenn Ford and

Whereas From 1923 when he first engaged in practice in Endicott, N. Y. he rapidly gained emimence and proficiency in his chosen specialty of X-ray serving as active Roentgenologist at Ideal and Wilson Memorial Hospitals, 1927–1939 and.

WHEREAS The American Board of Radiology and the American Roentgen Ray Society honored him with membership during his brief years of practice and he served as Chief of Staff of Ideal Hospital 1938–1939 and,

WHEREAS Those who were associated with him and countless others who came in contact with him socially and professionally attest to his ability, gentlemanly bearing and sincere devotion to his specialty coupled with a loyalty deeply ingrained through several years of pleasant contacts,

BE IT THEREFORE RESOLVED, That the Broome County Medical Society wishes to express to the family of Dr. Glenn Ford its deep sense of less of so promising a physician and,

BE IT THEREFORE RESOLVED, That a copy of these resolutions be sent to the family of Dr. Glenn Ford, a copy to the American Roentgen Ray Society, and a further copy spread on the minutes of the Broome County Medical Society.

It is with regret that the Journal announces the death of Aristide Busi, Professor of Radiology in the Atheneum of Rome, Founder and Emeritus Honorary Member of the Italian Society of Medical Radiology, which occurred in Rome on October 30, 1939.

## SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

## MEETINGS OF ROENTGEN SOCIETIES\*

United States of America

AMERICAN ROENTGEN RAY SOCIETY

Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Hotel Statler, Boston, Mass., Oct. 1-4, 1940.

AMERICAN COLLEGE OF RADIOLOGY

Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Next Annual Meeting: Commodore Hotel, New York City, June 12, 1940.

Section on Radiology, American Medical Association Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: New York City, June 10-14, 1940.

RADIOLOGICAL SOCIETY OF NORTH AMERICA

Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting, 1940: To be announced. RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SOCIETY

Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May,

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September. Section on Radiology, Illinois State Medical Society

Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill. Next meeting Peoria, Ill., May 21-23, 1940.

RADIOLOGICAL SECTION, Los ANGELES Co. Med. Soc. Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each

month at County Society Building.
Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.
BROOKLYN ROENTGEN RAY SOCIETY

Secretary, Dr. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY

Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to May inclusive at the Hotel Sherman.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY

Secretary, Dr. H. A. Mahrer, 10515 Carnegie Ave. Meets at 6:30 P.M. at Mid-Day Club rooms on fourth Monday each month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB

Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY

Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY

Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY

Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

ILLINOIS RADIOLOGICAL SOCIETY Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meetings held quarterly, on the fourth Sunday of the month.

Indiana Roentgen Society
Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annually.

KENTUCKY RADIOLOGICAL SOCIETY

Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville. Meets annually in Louisville on third Sunday afternoon in April.

LONG ISLAND RADIOLOGICAL SOCIETY

Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS

Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing. Three meetings a year, Fall, Winter, Spring. MILWAUKEE ROENTGEN RAY SOCIETY

Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis. Meets monthly on first Friday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY

Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

Nebraska Radiological Society

Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets first Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY

Secretary, Dr. W. J. Marquis, 198 Clinton Ave. Newark. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by president.

NEW YORK ROENTGEN SOCIETY

Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY

Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY

Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November. PACIFIC ROENTGEN CLUB

Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY

Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Annual meeting, June, 1940, exact time and place to be decided.

PHILADELPHIA ROENTGEN RAY SOCIETY

Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY

Secretary, Dr. H. W. Jacox, 4800 Friendship Ave., Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y. Secretary, Dr. S. C. Davidson, 277 Alexander St., Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

St. Louis Society of Radiologists

Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY

Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

<sup>\*</sup> Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

SOUTH CAROLINA X-RAY SOCIETY

Secretary, Dr. Hillyer Rudisill, Jr., Roper Hospital, Charleston. Meets in Charleston on first Thursday in November, also at the time and place of Scuth Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY

Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY

Secretary, Dr. H. C. Harrell, 517 Pine St, Texarkana, Texas.

University of Michigan Department of Roentgen-OLOGY STAFF MEETING

Meets each Monday evening from September to June,

at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:20-5:00 P.M., Room 301, Service Memorial Institute.

VIRGINIA RADIOLOGICAL SOCIETY

Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY

Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday of each month at the College Club, Seattle.

#### CUBA

Sociedad Cubana de Radiologia y Fisioterapia Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

#### BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY

Meets monthly on third Thursday, from November to June inclusive, at 8:15 p.m., 32 Welbeck St., London.

SECTION OF RADIOLOGY OF THE ROYAL SOCIETY OF MEDICINE (CONFINED TO MEDICAL MEMFERS) Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

FACULTY OF RADIOLOGISTS

Secretary, Dr. Barbara M. Key, 32 Welbeck St., London,

W.I, England.

SECTION OF RADIOLOGY AND MEDICAL ELECTRICITY, AUS-TRALASIAN MEDICAL CONGRESS

Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

RADIOLOGICAL SECTION OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION

Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussion. CANADIAN ASSOCIATION OF RADIOLOGISTS

Secretary, Dr. A. C. Singleton, Medical Arts Bldg., To-

ronto, 5, Ontario.

Section of Radiology, Canadian Medical Association Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S. RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL

Association Secretary, Dr. Colin Anderson, Invercargill, New Zea-

land. Meets annually.

## CONTINENTAL EUROPE

BELGIAN SOCIETY OF ROENTGENOLOGY

Secretary, Dr. J. Boine, Avenue des Ailiés, 134, Louvain

Meets monthly on second Sunday at d'Egmonds Palace,

Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France

Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris. Société Suisse de Radiologie (Schweizerische Rönt-GEN-GESELLSCHAFT)

Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.

Secretary for German language, Dr. Scheurer, Molzgasse, E el. Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiol-OSIE MEDICALE

Neets monthly on fourth Tuesday, except during month of August and September, 12 Rue de Seine, Paris.

ASSOCIATION OF GERMAN ROENTGENOLOGISTS AND RADI-OLOGISTS IN CZECHO-SLOVAKIA Secretary, Dr. Walter Altschul, German University,

Prague, 11.52.

DEWTSCHE RÖNTGEN-GESELLSCHAFT (GESELLSCHAFT FÜR BENTGENKUNDE UND STRAHLENFORSCHUNG)

Meets innually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforsel er und Aerzte.

Fernament Secretary, Professor Dr. Haenisch, Klopstock-

s rasse 10, Hamburg, Germany.

SÜE- UNE WESTDEUTSCHE RÖNTGENSELLSCHAFT

Meets annually in different cities.

NOAD UND OSTDEUTSCHE RÖNTGENGESELLSCHAFT

Meets annually in different cities.

DUTCH SOCIETY OF ELECTROLOGY AND ROENTGENOLOGY Holds wo meetings a year in Amsterdam, one in the Sering and one in the fall.

SOCIETA \*TALIANA RADIOLOGIA MEDICA

Secretary, M. Ponzio, University of Turin, Prof. Turin Societatea Romana de Radiologie si Electrologie

Eecretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania.
Meets second Monday in every month with the ex-

ception of July and August.

AL\_RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St. Scoretaries, Drs. S. A. Reinberg and S. G. Simonson,

Meets annually.

LENINGRAD ROENTGEN RAY SOCIETY

Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Instinute of Roentgenology and Radiology, Leningrad. Masseaw Roentgen Ray Society

Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konolæjevsky. Meets monthly on first Monday at

# o c.ock.

POLISH SOCIETY OF RADIOLOGY

Searctory, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsow. Meets annually.

WARRAW SECTION, POLISH SOCIETY OF RADIOLOGY Szeretary, Dr. B. Krynski, 11 Zielna St. Meetsconce a month except in the summertime. Scandinavian Roentgen Societies

The S. andinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the folwing societies, with exception of the Denmark Society, xeets every second month except in the summer ime:

SOCIETY OF MEDICAL RADIOLOGY IN SWEDEN

Meets in Stockholm.

SCELETY OF MEDICAL RADIOLOGY IN NORWAY Meets in Oslo.

SCRIETY OF MEDICAL RADIOLOGY IN DENMARK

Secretary, Dr. G. Biering, Copenhagen.

Meets the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State institute of Roentgenology.

SCIETY OF MEDICAL RADIOLOGY IN FINLAND

Meets in Helsingfors.

VEENIA ROENTGEN SOCIETY

Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Aberstrasse 4.

JAPAN X-RAY ASSOCIATION

orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

KINEL BOENGEN-ABEND SOCIETY
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan Meets bi-monthly on third Sunday.

## BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

Points of Interest

The following communication was sent to the Inter-Society Committee state representatives on November 15:

Once there was a boy who cried, "Wolf!" so often when no wolf came that the men who heard him paid no attention. Then one day, the wolf came and the men were sorry they had not heeded the boy's warning.

For several years, radiologists have warned surgeons, internists, obstetricians, urologists, orthopedists, et al., that hospitals would one day dominate all medicine if a few specialties were sacrificed to economic convenience. If hospitals could practice radiology, it has been said, they could likewise practice other specialties. If radiology is included as a hospital benefit in group hospitalization plans, there is nothing to prevent the inclusion later of other services.

Radiologists have appealed for help from their colleagues and warned of dangerous consequences to all medicine if such help were not forthcoming. Sometimes such help has not been forthcoming.

Well, here comes the wolf!

David B. Skillman is Chairman of the Trustee Section of the American Hospital Association. He is a hospital administrator from Easton, Pennsylvania. At the recent annual meeting of the American Hospital Association in Toronto, Canada, Mr. Skillman delivered himself of a paper on medical and hospital economics.

The following is quoted from a report which appeared in *Modern Medicine* for November, 1939:

"Salaries for Doctors.—A proposal that hospitals establish faculties of doctors with definite salaries has been forwarded as a means to combat socialized medicine. Mr. David B. Skillman, Chairman of the Trustee Section of the American Hospital Association, would fix the salaries starting at \$1,800 to \$2,000 a year for young, unmarried practitioners, and advancing to \$10,000 or \$12,000 for men of advanced standing.

"The hospitals would submit their bills according to a published scale of prices. The plan is merely an expansion of the group hospitali-

zation plan to take in medicine, and would eliminate state, county, and federal support."

This to combat socialized medicine, says Mr. Skillman. Indeed! One might say also that Finland could have avoided invasion by the Soviets if she had asked for military occupation by the Nazis. Individual determination and freedom is sacrificed one way or the other.

\* \* \* \*

In its many and laudable activities for the protection and preservation of the private practice of medicine, the *Kansas State Medical Society* has never failed to apply its principles to all branches of the profession.

Recently, the Committee on Tuberculosis of the Kansas State Society discussed the question of consultation service in the interpretation of roentgenograms when such is desired by individual physicians. The following resolution was adopted:

- 1. That the committee believes the principles of the private practice of medicine should be followed in the handling of X-ray consultations.
- 2. That the Committee urges physicians who desire X-ray consultations on tuberculosis cases to utilize the services of the radiology specialists of the state.
- 3. That the radiologists of Kansas at a meeting held on January 15, 1939, agreed they would provide this service without charge to any patient who is deemed to be indigent by the attending physician, and that, therefore, no problem is presented in this connection.
- 4. That in the instances of X-ray consultations desired for non-indigent patients the Committee recommends that the services of a radiologist be utilized with the expectation of paying a fee for that service.

A fee of \$2.50 has been recommended as the proper sum to charge for roentgen examinations in connection with tuberculosis in indigent patients. The fees for nonindigent patients are to be governed by the usual and customary charges in the community.

Radiologists concerned about the ultimate destiny of the specialty of radiology in the citadel of medicine should be interested in the following news letter from *Bucharest* which was published in the *Journal of the American Medical Association* almost two years ago:

## Regulation of the Title X-Ray Specialist

"The position of the X-ray specialists has undergone an unfavorable change in recent years. The number of X-ray installations is growing by leaps and bounds, owing to the fact that the peasants falsely believe that only physicians who own an X-ray apparatus can establish a good diagnosis. General practitioners, almost without exception, own X-ray sets, even in villages where there is no electricity and where they have to work their sets with gasoline motors. This situation affects badly the X-ray specialist, who receives his patients from the general practitioners. Another drawback for the X-ray specialist is that the general practitioner shows on his name plate that he possesses an Xray apparatus, so when a patient drops in, seeing the name plate, for a roentgenogram of a dislocated wrist, he does not refer the patient to the X-ray specialist but keeps the case for himself. The X-ray specialists held a conference to find a remedy for this situation. The result was that the Supreme Health Council made the following resolutions:

- "1. Physicians who have an X-ray apparatus in their office with the aim to establish diagnoses and control the progress of certain diseases on their own patients must not call themselves specialists in radiology and they are not entitled to display on their name plates and on their prescriptions that they have an X-ray apparatus or that they deal with radiologic treatment, and they are not entitled to issue X-ray reports.
- "2. Only such physicians can be acknowledged as X-ray specialists as those who have gained their diploma in Rumanian universities and received a license to call themselves 'specialist in radiology.'
- "3. Physicians who in 1930 had been in roentgenologic practice for five years receive the title of specialist simply on the verification of the city medical officer of health."

The Council of the Ohio State Medical Association discussed the status of group hospitalization insurance in that state during a recent meeting. The following statement of policy was adopted and copies were transmitted to all county medical societies:

## Statement of Policy

It is easential that the medical profession take an active interest in all proposals or programs affecting the care of the sick. Leadership must be assumed by state and local medical societies

Real zing that there is increasing public interest in programs to provide hospitalization on a voluntary insurance basis and anticipating the expansion of group hospitalization programs in Thio under the provisions of enabling legislation enacted at the recent session of the Ohio General Assembly, the Council of the Ohio State Medical Association believes that all county medical societies should give the question of group hospitalization immediate and earnest consideration.

Inasmuch as hospital service programs are administered through local units, the responsibility for considering medical questions which may be involved rests with the individual county medical society. The Council suggests that county medical societies in counties where hospital service programs are now in operation and county medical societies where such programs are under consideration carefully evaluate the contracts being sold, or which are being formulated by hospital service associations. Special attention should be given to the coverage provisions of such contracts.

The Council recommends that county medical societies use the following principle as a guide in exaluating contracts and in conferences with hospital service association representatives:

The subscriber's contract should exclude all medical services. Contract facilities should be limited exclusively to hospital facilities such as bed, beard, operating room, medicines, surgical dressings, general nursing care, and services of intern and resident staff in assisting the subscriber's attending physician.

If the above principle is complied with by all local hospital service associations in formulating a schedule of benefits, the result would be a certain uniformity of policy and procedure

throughout the state, efficiency in administration, and absence of misunderstanding.

The medical profession of Ohio believes that group hospitalization programs, in the hands of reputable and efficient administrators, are of definite public benefit, providing such programs are limited to hospital services and do not include medical services, which inclusion would have an undesirable effect on the practice of medical specialties in hospitals and on the quality of the service rendered. Group hospitalization plans operated in accordance with the above principle should have the active cooperation of the medical societies in the localities in which they operate.

\* \* \* \*

The following is from the New York Medical Week:

## Danger Ahead

A local judge recently imposed a fifteen-dollar fine, for passing a red light, on a motorist who admitted illiteracy. At the same time he criticized severely the system which permits drivers who cannot read or write to operate cars. No matter how competently a motorist handles his machine, he is not a safe driver if he cannot read certain warning signs.

In technical fields allied to medicine there is a parallel to this situation. Many registered physiotherapists consider themselves qualified to practice medicine because they can operate their apparatus, although they are completely unable to read danger signals in a patient's condition or make a diagnosis. It is a sad and well-known fact that physicians often employ commercial X-ray and clinical laboratories whose technicians do not know how to interpret the signs set before them.

Whether in driving or medical practice, a certain amount of knowledge is necessary besides mastery of an inanimate machine. It is doubtful, however, whether the illiterate motorist is nearly as dangerous as the lay technician who takes to the medical road without being able to read warning signs.

\* \* \* \*

Dr. E. H. Skinner and Dr. F. F. Borzell have been selected to serve on the Executive Board of the National Physician's Committee for the Extension of Medical Service. The formation of the Committee was stimulated by earlier activities opposing governmental regimentation of medicine carried on by publisher Frank Gannett's National Committee to Uphold Constitutional Government. The present Committee, however, has no connection with the Gannett Committee, nor with the American Medical Association. The stated objectives of the Committee are to cooperate "with lay and medical institutions and groups, interested in the preservation of national health, and to make more generally known the achievements and to safeguard the independence of American medicine."



## **BOOK REVIEWS**

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

OUTLINE OF ROENTGEN DIAGNOSIS: AN ORI-ENTATION IN THE BASIC PRINCIPLES OF DIAG-NOSIS BY THE ROENTGEN METHOD. By Leo G. Rigler, B.S., M.B., M.D., Professor of Radiology, University of Minnesota, Minneapolis, Minnesota. Atlas edition. Cloth. Price, \$6.50. Pp. 212, with 254 illustrations shown in 227 figures, presented in drawings and reproductions of roentgenograms. Philadelphia: J. B. Lippincott Company, 1938. (Also furnished in a Student Edition, 212 pages, \$3.00.)

This textbook of Rigler's is exactly what it purports itself to be, an outline and not a complete textbook. The method of presentation is that of a summary or of an outline for lectures and there are few words wasted in pictorial description. In the ideal textbook (yet to be written) all possible conditions and every conceivable variation must be described accurately and pictured perfectly both by description and by photographic copying of the highest quality. Rigler's Outline considers only the more common conditions, giving them their proper relative emphasis, it is true, but leaving out many essentials.

His presentation is precise and concise, at times to the point of too much brevity. The material is very well arranged and subdivided, easy to skim through and already summarized, ideal for a harried medical student, but not for the graduate intending to enter roentgenology, or for the roentgenologist. Of particular value to the medical student are the considerations of roentgenological methods, technical procedures, normal anatomy and possible errors, which precede most of the main anatomically arranged chapters. Of even more value are the summaries at the end of each section, where Rigler gives his honest opinion as to the "value of x-ray examination" in that particular condition or part. These "values" are in the main correct, reasonable and not-too-enthusiastic estimates of the usefulness of the roentgen method, a matter which is often very uncertain in the average student's mind.

The illustrations are good in two particulars,

poor in others. (The book has two editions, one with the illustrations or "Atlas" and the other one without this very necessary feature). The good points are that all of the roentgenograms are presented in their proper value of blacks and whites, i.e., negatives, thus avoiding the additical confusion to students of having to interpret some roentgenograms as positives, others as negatives. Another good point is the excellert use of outline or line drawings, in the section on the heart particularly, further avoiding confusion. Some of the defects in illustrating are that text and figure are separated, all of the Illustrations being printed on different paper and bound together at the back of the book. This adds confusion, requiring frequent turning of pages, loss of continuity and mental exasperation is trying to combine text and pictorial images. The reproduction of roentgenograms is fairly and, but the "original technique" of illustrating most of the bone lesions is sadly lacking in Jamty and in detail. The artist has given all of the bones a peculiar stippled appearance which may be the way they look to her, but to the informed reader it would seem that all of the cases suffered from an advanced degree of splenic anemia, and it must be confusing to the average student.

The book is well set up mechanically, running to 212 pages including the index, and 122 unnumbered pages of illustrations, with the figures or strawings all on the right hand page and descriptive text on the opposite page, with only the common conditions pictured in the 227 illustrations. The book could have been smaller as there is an unusually wide margin for the text, 3.5 cm. at the sides and 5.5 cm. at the bottoms of the pages. The type is clear and easy to read, the headings are uniform and well spaced, and the left marginal offsets correspond accurately to the subheadings. There are surprisingly few typographical errors for a first edition, but there are several colloquialisms which might be eliminated, such as "slow growing." operated stomach," "perinephritic abscess" instead of the more grammatically correct "slowly growing," "postoperative stom-

ach" and "perinephric abscess."

On the whole, this book is a good one for medical students—ar "Orientation in the Basic Principles of Diagnosis by the Roentgen Method," as the author's subtitle puts it, and particularly valuable if combined with the actual demonstration of roentgenograms in more detail and variety than is done in the "Atlas" portion of the book. But as a text for graduate study, for reference, or for consultation, it is decidedly incomplete.

M. C. S.

ROENTGEN TECHNIQUE. By Clyde McNeill, M.D. Cloth. Price \$5.00. Pp. 315, with 268 illustrations. Springfield, Illinois: Charles C Thomas, 1939.

The author's purpose has been to produce a practical reference book of roentgen technique and this has been carried out in a very excellent manner. For each technical procedure he has reproduced a photograph illustrating the position together with either a finished roentgenogram or a line drawing from the roentgenogram, diagrammatically illustrating the desired endresult. On the opposite page to these he gives the technical factors, a description of the position, the purpose of exposure and/or the salient points bearing thereon, together with a bibliography in certain cases where a special, more detailed knowledge may be desired of the procedure by the reader.

The book is divided into four parts. The first deals with the head, the second with the extremities, the third part with the trunk, and the fourth part deals with exposure techniques and methods of preparation of opaque media, etc. In the first part the author has a series of drawings indicating the angle of projections in the various head positions. These are very comprehensive. Following these he proceeds to explain the various routine positions for roentgenography of the head. The routine encephalographic positions are shown. Special mention should be made of the section on dental roentgenography and foreign body localization in the eye. Measurement of the pineal body position is also discussed. The second part, dealing with the extremities, has a section on bone development, anatomical variations and accessory bones, which precedes the routine explanation of positions. The section on the trunk, after dealing with the skeletal portion, outlines the procedures for roentger ography of the chest, abdomen, and the special examinations where

opaque material is used. Pelvic mensuration is also discussed as well as tomography and kymography.

In his preface, the author points out that relatively little space was devoted to practical exposure technique since this is the portion that most quickly becomes obsolete.

Obviously in a work which attempts to be as comprehensive as this, minor omissions occur which are not to be considered of too much importance. Often various individual laboratories have their own favorite methods which might be missed by one too critical. It is to be assumed that the reader realizes that often the standard positions cannot be accomplished because of the condition of the patient, particularly in fracture work. For example, one is reminded, when reading the portion on roentgenography of the hip and upper femur, that the standard positions here which are described are often very difficult to obtain because they are usually used for fracture of the hip. If fracture is not present, then the extremity can usually be manipulated into the position described by Hickey some years ago, which gives as good a lateral view of the femoral neck as any position. This position is not mentioned.

Further, nothing is said about routine work with the portable apparatus at the home or on the hospital ward.

Again the necessity for making several exposures of the spine in the anteroposterior position to compensate for curvatures which might be present is not stressed. These are, however, not very serious omissions.

Perhaps a little too much stress has been laid on pelvimetry and cephalometry since it is now generally recognized that measurements *per se* are of little value.

McNeill has done an admirable work. His efforts represent one of the best monographs of this kind that has been added to the literature in recent years. The construction of the volume comes up to the usual high standard of the publisher.

PAUL C. SWENSON

CLINICAL ROENTGEN THERAPY. Edited by Ernst A. Pohle, M.D., Ph.D., F.A.C.R., Professor of Radiology, Chairman, Department of Radiology and Physical Therapy, in the University of Wisconsin, Madison, Wisconsin. Foreword by George W. Holmes, M.D., Roentgenologist to the Massachusetts General Hospital and Clinical Professor of Roentgenology in Harvard Medical School, Boston, Mass. Cloth. Price \$10.00. Pp. 819, with 199 illustrations. Philadelphia: Lea & Febiger, 1938.

A glance at the index of this book shows that it begins with "Abortion produced by roentgen rays" and ends with "Xanthomatosis." This simple fact indicates that the book covers a wide field. It also indicates the wisdom of the editor in choosing a number of well known contributors, inasmuch as a single individual obviously lacks the background of training and experience to cover the entire field adequately. By the same token the reviewer is likewise handicapped in his appraisal of all of the subject matter.

One might well question the wisdom of the editor in divorcing "Clinical Roentgen Therapy" from "Theoretical Principles of Roentgen Therapy." The two subjects are treated in separate volumes without anything in the respective titles to indicate that they are in reality companion works. The former is not complete without the latter. Taken together the two give a well rounded exposition of the present status of roentgen therapy which should prove a great boon to teachers, students and practitioners in this highly important field. The latter, particularly, not only owe it to themselves and their patients to use the books liberally, but they also owe it to radiology as a whole in order that the editor and contributors may be encouraged to issue such future editions as may be required to keep the work abreast of future developments.

THOMAS A. GROOVER

RADIATION THERAPY: ITS USE IN THE TREATMENT OF BENIGN AND MALIGNANT CONDITIONS. By Ira I. Kaplan, B.Sc., M.D., Clinical Professor of Surgery, New York University Medical College; Director, Radiation Therapy Department, Bellevue Hospital, New York; Director Division of Cancer, Department Hospitals, City of New York, etc. Cloth. Price, \$10.00. Pp. 558, with 198 illustrations. New York: Oxford University Press, 1937.

Kaplan's enormous clinical experience is reflected in this excellent book. The use and methods of radiation therapy, as found in the busy and highly specialized cancer clinics, or in the general and private practice of radiology are ably presented.

Beginning with a brief historical development of radiation therapy and ending with two unusual chapters: nursing care of patients with malignant conditions, and suggestions as to the organization and equipment of a radiation therapy department. The book clearly and consisely covers the vast field of therapeutic radiology.

One unusual feature is the chapter on the use of electrosurgical currents, a much neglected but essential modality in the treatment of many diseases.

The body is systematically divided into regions, and due consideration is given both benign and malignant lesions. One or several elective techniques using roentgen rays or radium are carefully and clearly presented so that the reader has no difficulty in following them. The individual requirement of the patients or the available equipment determines the exact type of therapy utilized

There are many good illustrations. The radiologist will find the book a useful and valuable text.

## R. RHETT RATHBONE

DESABILITY EVALUATION. PRINCIPLES OF TREATMENT OF COMPENSABLE INJURIES. BY Earl D. McBride, B.S., M.D., F.A.C.S., Assistant Professor in Orthopedic Surgery, University of Oklahoma School of Medicine; Attending Orthopedic Surgeon to St. Anthony's Hospital; Associate Orthopedic Surgeon to Wesley Hospital, etc. Second edition revised. Cloth. Price, \$8.00. Pp. 623, with 374 illustrations. Philadelphia: J. B. Lippinectt Co., 1938.

This comprehensive 623 page volume is written as a reference for the physician who finds it necessary to participate in legal controversies dealing with compensation for industrial injuries. The provisions of workmen's compensation laws as they are applied in each province of Canaca and each state of the United States are giver in detail in the first portion of the book. As attempt is then made to standardize and evaluate the various types of disability with machematical accuracy, and the methods of examination on which the evaluation depends are described for each portion of the body.

The loss of function and resulting disability following partial or total ankylosis are considered separately for each joint in the skeleton and another large section deals with the temporary or prolonged interference with useful

activity resulting from the proper or improper healing of all well known fractures. The industrial back receives its share of attention and separate chapters are devoted to nerve injuries, amputations, head injuries, injuries of the eye and ear, burns and hernia.

Proper methods of treatment are illustrated in each instance and frequent reference is made to the importance of roentgen studies as a protection against malpractice suits. Unfortunately roentgenograms are referred to as "x-ray pictures" in many of the charts copied from exhibits prepared by the American Medical Association but on the whole the illustrations are well chosen to illustrate the points made in the text. Although the determination of disability is a clinical rather than a roentgenological problem any roentgenologist who examines industrial injury cases can find in this treatise much valuable information not included in the curricula of most medical schools.

CHARLES L. MARTIN



## DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 105 Rutledge Ave., Charleston, S. C.

## AN INTRANASAL CONE FOR THE CHAOUL APPARATUS

By LESTER HOLLANDER, M.D., and JCSEPH M. SHELTON, M.D.
From the Pittsburgh Skin and Cancer Foundation
PITTSBURGH, PENNSALVANIA

IN THE past two years we have been using the Chaoul apparatus in the treatment of intracavitary neoplasms. During this time we have treated 5 patients suffering from intranasal malignant disease, including 2 of melanocarcinoma.

The ordinary cones are much too large to permit introduction into the nasal cavity, thus it was necessary to devise an auxiliary cone for this purpose.

This cone consists of a piece of nickelbrass metal tubing I cm. in outside diameter, having a wall thickness of I mm. This tubing is 3 cm. in length and is imbedded in a molded lead base attached to a short sleeve which fits into the aperture of a standard 3 cm. cone. The over-all length of the come is 4.25 cm., increasing the targetskin distance to 7 cm. This increased distance and the narrowed aperture decreases the roentgen output to 20–35 r per minute, thus necessitating a daily exposure of fifteem to twenty minutes to reach our usual dose of \_00 to 500 r daily.

In all cases there has been a marked regression in the local growth although the 2 melanomas terminated fatally. In spite of the fact that the radiation is directed "blindly" to a certain extent, our rhinologist reports that we have been able to obtain satisfactory local results without extensive damage to the adjacent normal mucosa.



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## ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

## ROENTGEN AND RADIUM THERAPY

HERNAMAN-JOHNSON, F. The after-care of patients suffering from breast cancer. Brit. 7. Radiol., May, 1938, 11, 297-310.

A large proportion of all cases of breast cancer will be dead within five years. Metastases in microscopic form are already present in a large proportion of breast cases when the primary tumor is first recognized. The five year survival statistics have been greatly improved by postoperative radiation treatment, but the ultimate mortality rate from cancer of the breast has not been affected.

Very great advances have occurred in the matter of alleviating the lot of the breast cancer patient. We must seek to prolong to the uttermost the lives of these patients, provided we can make these lives useful and happy. The majority of patients suffering from cancer of the breast should be told the truth at the first suitable moment after microscopic examination has confirmed the diagnosis. The expression "aftercare" means the care of the patient after the primary growth has been dealt with.

Efficient supervision of all breast cases from the time of the operation onwards is best carried out in any given area by one man rather than by fifty. As the physician in charge of radiotherapeutics is the person who will inevitably be called upon to deal with them when they go wrong, logic demands that he should have the supervision of them from the comr.encement. Systematic after-care can best be carried out by the creation of a special clinic, to which all patients are sent as soon as possible after operation. The author established an after-care clinic at the Croydon General Hospital three vears before presenting this article and, of the 33 patients registered three years ago, 19 patients are still attending the clinic. The advantages to be gained by the establishment of an after-care clinic are summarized. One of the advantages is the lessons to be learned from the necessarily closer study of each patient.

For purely prophylactic treatment in good risk operable cases, heavy dosage carried to a point where healthy tissues may be damaged is not justified. When there is localized recurrence, heavy dosage over a strictly localized area is valuable as a palliative. For practical purposes, breast cancer in its later stages must be regarded and treated as a general disease.

Attempts have been made for many years to find some drug which would be selectively destructive to malignant cells. The alternative is to find some way of stimulating tissue resistance. Todd, of Bristol, believes that the resistance mechanism is to be found in the reticuloendothelial system. He further believes that if certain compounds of selenium be introduced into the circulation, the element finds its way into this system, and can thereafter be activated by means of roentgen rays, and that by this means tissue resistance to cancerous invasion can be stimulated. The author cites several cases which showed marked improvement following Todd's method of treatment. He believes, however, that the results are too uncertain to warrant the use of this method in routine hospital practice.

Mention is made of the use of biochemical tests as a guide to treatment and prognosis in cancer of the breast. The test employed has been the differential sedimentation test. In known cases of the disease it has a value in indicating the kind of fight which the patient is putting up against the disease.

Local recurrence in the skin or in the axilla can be cured or held in check by irradiation. Invasion of the supraclavicular glands may also be confined to this site by heavy roentgen-ray dosage. Swelling of the arm which does not improve with heavy doses of roentgen radiation to the axilla may be relieved by surgery.

Radiotherapeutics, if it is to progress, must not ally itself exclusively with surgery and physics, but must look to medicine for guidance and more particularly to those branches of it which are known as endocrinology and biochemistry.—S. G. Henderson.

Sosman, Merrill C. The roentgen therapy of pituitary adenomas. J. Am. M. Ass., Sept. 30, 1939, 113, 1282-1285.

There are three important fundamental principles to be established before consideration of the results of roentgen therapy alone. We must judge our results by the patient's restoration to health, a return to a normal mode of living and, particularly in the chromophobe type of ade-

noma, by restoration of vision. With modern accurate penetrating radiation one can and does give larger and more accurately measured total doses, spreading treatment over a longer period and using more portals, and can justifiably expect from present indications a greater effect on the tumor. Pituitary adenomas are extremely variable in their rate and direction of growth, and their effect on health and vision and, like all adenomas of endocrine glands, are liable to spontaneous remissions. It might be more valuable to analyze and compare failure rather than to consider only good results.

Sevem of 8 patients with the chromophobe type of adenoma received marked benefits from the irradiation, both as to restoration of vision and as to return of the patient to normal living. The duration of improvement in the cases has lasted from three to five years, with no recurrences so far. Failures occur in patients with advanced extensive lesions, either invasive in bone or with large intracranial extensions. Failures may also occur in cases in which the tumor has been pressing on the optic nerves or chiasm so long that it has produced atrophy of the fibers. Cystic tumors, which formed 17 per cent of Cushing's 260 chromophobe tumors, are said not to respond to irradiation.

The dangers from or following irradiation are real our infrequent. Henderson found in one case extensive adhesions between the adenoma and the chiasm, which prevented a satisfactory surgical removal. He assumed the adhesions to be due to extensive irradiation elsewhere for more than a year before operation. Sosman has seen an acute hemorrhagic cyst develop after a fairly heavy single roentgen treatment for recurrence after operation. Cataract formation is a definite possibility after heavy (and perhaps careless irradiation. Experiments lead one to believe that the nervous tissue of adults will stanc a dosage up to 6,000 roentgens in any one area. One should keep below this dose, thereforz, to avoid injury to the vessels and subsequent brosis, gliosis or necrosis. While roentger therapy is being tried, the failure promptly to remove the pressure on the optic chiasm may possibly result, with unsatisfactory responses, in a change from temporary relievable blindness to permanent optic atrophy due to degeneration of the nerve fibers. Acidophil tumors and acromegaly respond more readily to irradiation than the chromophobe type. The majority of them can best be treated by irradiation, and they are much more liable to spontaneous remissions and waves of activity and inactivity. These tumors grow slowly and the eventual result is in doubt for many years. The most distressing symptom of nearly all the patients irradiated was headache, and this was definitely improved or entirely relieved in 90 per cent of 28 cases.—S. G. Henderson.

Bartsch, H., and Wachner, G. Herzgefässschädigungen und ihre Prophylaxe bei protrahiert-fraktioniert bestrahlten Tumoren der oberen Luft- und Speisewege. (Cardiovascular injuries and their prophylaxis in protracted fractional irradiated tumors of the upper air and food passages.) Strahlentherapie, 1938, 62, 339–342.

While cardiovascular injuries have been repeatedly demonstrated experimentally following intensive irradiations, the data regarding such injuries on humans are meager. Coutard and Lavedan were the first to call attention to this phenomenon. They have observed numerous patients with symptoms of dyspnea, shortness of breath, and muscular weakness. Physically they were able to demonstrate tachycardia, a fall of blood pressure, a decrease of the blood pressure amplitude, intensification of heart murmurs, etc. In benign cases these phenomena disappeared after a few weeks, while in severe cases the improvement was delayed and not infrequently death occurred.

Parade was able to demonstrate, on the basis of a study of 2 cases of mitral stenosis, the development of severe cardiac disturbances as a result of roentgen irradiation which led to auricular fibrillation and absolute ventricular arrhythmia. One of these cases was treated for a tumor of the thorax and the other for carcinoma of the uterus; in the first case one had to deal with a direct and in the second with an indirect effect of the irradiation.

Schinz and Zuppinger have called attention to the danger or threat to the circulation or to the body as a whole during the Coutærd method of irradiation of tumors of the upper air and food passages. Eight of the 30 cases irradiated for carcinoma of the pyriform sinus died at the end of irradiation from pulmonary and circulatory complications. In one case a latent decompensation was transformed following the irradiation into a manifest decompensation. Also Lambadaridis was able to demonstrate untoward effects on the circulation under the

influence of Coutard's method of irradiation. These effects were expressed in the form of a fall of the blood pressure, a decrease of the amplitude, the appearance of extrasystoles and myocarditic disturbances. Some authors are of the opinion that the presence of a poor heart is a contraindication to Coutard's method of irradiation. Mayer reported the development of an acute cardiac weakness following irradiation.

These authors observed cardiovascular injuries in patients subjected to the protracted fractional method of irradiation of the tumors of the upper air and food passages. In 47 cases with predominantly carcinoma and occasionally sarcoma of the epi- and hypopharynx and of the larynx, with or without regional glandular metastasis, the irradiation was carried out as follows:

Daily the right and left cervical field, including the supraclavicular fossa and in cases of epipharynx tumors, also the cheeks, of an area of 50 to 150 sq. cm. were alternately irradiated, one field in the forenoon and the other field in the afternoon. The irradiation was given in the course of four weeks. The individual dose varied from 100 to 200 r with a zinc filter of 1 mm. and 40 cm. focus-skin distance. The total dose was on the average 7,500 r surface dose.

Before and after each irradiation an orthodiagram, pulse frequency, blood study and electrocardiogram were obtained. In a large number of cases a lowering of the blood pressure combined with a decrease of the blood pressure amplitude, an increase of pulse frequency, as well as changes in the electrocardiogram, were found pointing to a disturbance in the process of contraction, expressed in the electrocardiogram in the form of the intercallated part and a flattening of the T-wave. In individual cases disturbances in rhythm were also observed. The changes in the electrocardiogram were most pronounced towards the end of the irradiation but some of them were apparently capable of regression.

To verify these findings, a series of experiments was carried out on rabbits with and without exposure of the heart, and following the irradiation the changes in the heart were studied histologically. In many of these cases the histologic changes simulated those found in severe cases of toxic myocarditis. These authors are of the opinion that these changes in the heart are apparently the result of a decomposition of proteins and the changes appearing

in the electrocardiogram are interpreted by these authors as the result of the direct effect of the proteins on the myocardium; they believe that this effect is also responsible for the fall of blood pressure and the tachycardia. These authors are of the opinion that in a predominant number of cases treated in the above given manner the treatment is followed by an injury to the myocardium. In consideration of these findings, these authors recommend a prophylactic cardiac and circulatory treatment before the irradiation in order to prevent the possibility or danger of a cardiac or circulatory insufficiency. The so-called cardiac prophylaxis must not only be limited to measures of a general nature, but actually requires medicamentous treatment. They recommend digitalization even for a perfectly sufficient heart in order to prevent possible collapse following the roentgen treatment. In the clinic of these authors the prophylactic digitalization is carried out as follows:

Three days each week the patient is given a small dose of digitalis three times daily; in many instances the digitalis is given in the form of a liquid in amounts of 10 to 15 drops per dose An attempt is also made to improve the peripheral circulation by the prophylactic administration of caffein and similar substances (veritol, sympatol).

A comparison of the results obtained in two groups of cases, those treated prior to the roentgen therapy and those non-treated, has revealed the absolute value of this prophylactic treatment. Among the 20 cases treated in the above manner, only in one a fall of blood pressure of about 30 mm. Hg occurred, while in the remaining 19 cases the lowering of the blood pressure did not exceed 10 mm. Hg.; in 78 per cent of the non-treated cases symptoms of peripheral circulatory weakness appeared which came to manifestation in the form of a fall of blood pressure up to 65 mm. Hg. No change in the pulse frequency was observed in the treated cases while such a change was observed in 70 per cent of the non-treated cases. The work is concluded with the emphasis on the necessity of a corresponding prophylactic cardiac and circulatory therapy prior to the Coutard irradiation.—A. S. Schwartzman.

Weissig, Heinrich. Die Röntgentherapie der Erkrankungen des kindlichen lymphatischen Rachenringes. (Roentgen therapy of diseases of the lymphatic pharyngeal ring of children.) *Strahlentherapie*, 1938, 62, 480-496.

One hundred and thirteen of the 120 children irradiated because of hyperplasia of the tonsils could be followed up and the results obtained were as follows:

Children with pure hyperplastic tonsils presenting no signs of inflammation or no signs of a catarrhal affection responded best to the treatment 162.5 per cent cured and 25-28 per cent improved). Of the hyperplasia in exudative diathesis orly 37.5 per cent were cured and only 37.5 per ceat were improved, therefore 75 per cent were favorably influenced. Children with fibrous indurated tonsils resulting from repeated severe throat infections do not respond as well. In those where irradiation was employed 44.4 per cent were cured and 30 per cent were improved. Children who had a previous history of scarlet fever responded especially poorly to the radiation therapy. Of these only 10 per cent were cured and 20 per cent improved. In cases of chronic recurrent angina and pronounced fibrous induration of the tonsils, surgery is preferably indicated.—A. S. Schwartzman

NEGRU, D. Die Röntgenbehandlung der Basedowschen Krankheit. (Roentgen treatment of Basedow's disease.) Strahlentherapie, 1938, 62, 450-479.

The beginning of roentgen treatment of Basedow's disease dates back to 1902. It was the first internal disease in which roentgen treatment was employed so that it was the first disease in which deep roentgen therapy was used. Nevertheless even at present there is no uniformity of opinion regarding the indication of this method of treatment in relation to surgical treatment; similarly there is no uniformity of view regarding the technique to be employed. According to some authors, many small doses at long intervals of time are recommended while according to others, large roentgen-ray doses at shorter intervals of time seem preferable. The subject of roentgen treatment of Basedow's casease was extensively studied by the author in the course of the last fifteen years during which time 428 patients were treated. Of these 428 patients treated, 295 could be followed up for a given length of time. On the basis of the results obtained

from these extensive studies, the author comes to the following conclusions: Roeatgen treatment of Basedow's disease must be a functional therapy. Its purpose is to control the neuroendocrine disturbance in equilibrium which is represented by this disease. The functional disturbance in general seems to have as a material substrate a very labile biochemical construction which is changed and normalized by the roentgen rays irrespective in what direction the disturbance has occurred. This would explain the good results obtained from the same therapeutic agent in so different and frequently antagonistic conditions. It appears that there exists a definite difference in radiosensitiveness between the pathologic and normal biochemical processes whereby the former are considerably more radiosensitive. Because of the above it is more difficult to change the normal than the pathologic function of a cell. A selective process takes place which is comparable with that of the normal and the tumor cells in the destructive cytocaustic therapy.

The usual dose must not exceed \frac{1}{3} skin erythema dose per sitting. Two to three irradiations of the same field with a pause of about one week between the sittings are suggested. The thymus gland must be irradiated but not more than with  $\frac{1}{3}$  s.E.D. in one sitting. Depending on the volume of the struma the rays employed may be either hard or of medium hardness. No material difference is obtained from the use of a filter of 4 mm. aluminum or of 0.5 mm. of copper plus 4 mm. of aluminum. At least three series of treatments given in the course of four months are necessary in order to change the final effect of the treatment. The condition may be looked upon as cured when an absolute and permanent normalization of the pulse frequency, of the basal metabolism and of the body weight and a complete restoration of the working ability have been attained. The roentgen therapy produces no injury to the skin or to the larvnx nor adhesions of the thyroid gland if correct and purely functional doses have been employed. A systematic control of the basal metabolism protects against myxedema which is an extremely rare and easily curable complication. The indications of roentgen therapy of Basedow's disease are very wide. Since roentgen therapy is a harmless method, it is to be preferred in all cases where definite contraindications do not exist. The most important contraindications are: strumata with symptoms

of compression, a suspicion of a malignant degeneration, toxic adenoma which from the very beginning gives rise to severe toxic symptoms. In cases where irradiation of the thyroid gland and thymus remains ineffective, roentgen treatment of other glands of internal secretion should be tried (suprarenals, hypophysis, ovaries). If even this remains ineffective an operation is indicated. Severe cases represent no contraindication to roentgen therapy. The roentgen therapy must be instituted as soon as the basal metabolism decreases to plus 10 per cent. Roentgen therapy gives in about 40 per cent of all cases total or permanent cures. In nearly 80 per cent of all cases cures or improvements are obtained. Recurrences occur in about 10 per cent of the cases.—A. S. Schwartzman.

NEWMAN, WILLIAM W., and GARLAND, L. HENRY. The non-surgical treatment of hyperthyroidism complicating heart disease. Surg., Gynec. & Obst., Nov., 1938, 67, 632–639.

A combination of iodine and roentgen therapy for hyperthyroidism will result in 60 per cent of cures based on the disappearance of symptoms, economic restitution, a lowering of the basal metabolic rate to plus 10 or below, the pulse rate to 80 or below, and a gain of weight to near the former average. In another 28 per cent there is marked improvement so that there will be satisfactory results in over 80 per cent of cases. There is no direct mortality or complication, the patient is ambulatory, the effect is relatively rapid, and if the treatment fails surgery can always be employed. Its value for those who refuse surgery is obvious whatever the reason.

Data to support the above statements is given by the authors as sufficient to recommend this form of treatment though not in all cases necessarily the best. Their evidence is very convincing.

Medium or high voltage therapy is used with moderate filtration over a single anterior neck field. The trachea is protected by a narrow strip of lead rubber; 150–200 r, measured in air, is given every second or third day up to a total dosage of approximately 2,000 r. Iodine in the form of Lugol's solution is given three times a day (5–10 drops) from the start for amelioration of the symptoms until the irradiation effect has been produced in from three to six weeks.—*P. C. Swenson*.

Breitländer, K. Röntgentherapie des Ulcus callosum ventriculi und Ulcus pepticum jejuni postoperativum penetrans. (Roentgen therapy of callous ventricular ulcer and postoperative penetrating peptic jejunal ulcer.) Strahlentherapie, 1938, 62, 331–338.

The author discusses a certain method of roentgen irradiation of chronic gastric ulcer (situated on the lesser curvature) and postoperative peptic jejunal ulcer. The technique of irradiation is basically as follows:

A sum total of 1,000 to 1,500 r surface dose is given depending on the course of the individual sittings, each of 100 r/o given every other day, 40 cm. focus-skin distance, 4.5 r/m, 180 kv. This method of treatment was employed only on chronic cases some of which gave a history of ulcer of years' duration and in each case, including the severe ones, the treatment was carried out under ambulant conditions. This represents the essential preference of this method since in a predominant number of cases the patients were able to follow their occupations. With the exception of the occasional administration of a dose of papaverin and anasesthesinbelladonna powder, no other treatment was given. Depending on the case, the ulcers disappeared from two, four to six weeks after the beginning of treatment. The patients were observed clinically up to two years and 90 per cent of them remained free of symptoms during this time. Altogether 48 cases were observed in this manner, 2 of which had a postoperative jejunal peptic ulcer. This method of treatment is not unpleasant to the patients, it is without any danger and is inexpensive. This author is of the opinion that the protraction and fractionization is decisive for the results obtained. He further believes that the roentgen method of treatment of jejunal peptic ulcer is definitely preferable to other methods, especially to surgical methods of treatment and he is convinced that in chronic peptic ulcer of the lesser curvature as well as in postoperative jejunal peptic ulcer good permanent results are obtainable by this method of treatment in a large percentage of cases. The basic point of the problem is essentially the question of dosage and it would be very desirable to consider this problem more thoroughly.—A. S. Schwartzman.

Todd, T. F. Rectal ulceration following irradiation treatment of carcinoma of the cervix

utz: . Surg., Gynec. & Obst., Nov., 1938, 67, 617-631.

Ukerasion of the rectum following radiation treatment of carcinoma of the rectum is given the mame of "pseudo carcinoma" because of its resemblance to carcinoma on digital examination. Two types are described, one restricted to the secta wall and the other involving mainly the periroctal tissues, producing a rather tumor-ke perirectal induration. Biopsy may be necessary to rule out persistent or recurrent carcinoma. The etiology is essentially one of overdosage in the vaginal vault and a lengthy discussion of prophylactic measures is given; fixation of the radium applicators. checking of their position by roentgen ray, reduct on of the dose in cases of retroversion and the use of the knee chest position during the period of irradiation.

The histology of the two types of lesions suggests a common feature of vascular occlusion probably due to thrombosis of the smaller branches of the hemorrhoidal vessels. This eventually brings about infarction and ulceration. Treatment of the ulcerations and their complications is discussed in detail.—P. C. Swersen.

### MISCELLANEOUS

GLAUNER, R. Vegetatives Nervensystem und Röntgenstrahlen. (The vegetative nervous system and roentgen rays.) Strahlentherapie, 1938, 62, 1-72.

A study of the clinical observations and experimental results reported in the literature reveals that only in rare cases is a definite proof of an actual influence of the vegetative nervous system by roentgen rays available. It appears that the utilization of roentgen rays in the treatment of the vegetative nervous system is still n its early beginning stages so that data of this type must be critically evaluated. A further standy of the data reported in the literature incitates that the autonomous nervous system can be influenced by roentgen rays and hypotheses may be presented which would explain the mechanism of action of the radiation effect. Many local points of influence may be differentiated. Principally the following come under consideration: (1) the influence on the autonomous nerve endings of the skin, especially the skin capillaries; (2) the influence on the pre- or post-ganglionic nerve strands;

(3) the influence on the ganglion; (4) the influence on the suprarenals, and (5) the influence on the vegetative centers of the brain.

In regard to the influence on the nerve fibers it may be stated that such an influence has as yet not been proved and can hardly be considered. A paralysis of the peripheral medullated nerves can be obtained only from the use of extremely high doses of roentgen rays. The results obtained from the experiments carried out on non-medullated autonomous nerves are not conclusive and do not definitely show that they are sensitive to roentgen rays even though on the basis of their general physiological behavior it may be assumed that the nonmedullated nerves are more sensitive to roentgen rays than the medullated nerves. In spite of that, however, even for the non-medullated nerve fibers roentgen doses are necessary which could hardly be considered therapeutically. This path of influence on the nervous system must therefore at present be discarded.

Histologic changes in the suprarenals can be obtained only from the use of very large doses. At this point it may be mentioned that even after a direct irradiation of the suprarenals no effect on the blood pressure is demonstrable when the skin is not irradiated at the same time. The effect of irradiation of the suprarenals comes to clinical manifestation only in the cases when a simultaneous irradiation of the paravertebral ganglia is carried out.

The relations are entirely different in regard to irradiation of the vegetative brain centers. Here the effect of the irradiation is unquestionable even though the results are not uniform. It must always be remembered, however, that late injuries may occur and consequently extreme care must be used in irradiations of this type.

Suzuki demonstrated the great sensitiveness of ganglia to roentgen rays. It has been more or less definitely shown that the cholin liberated during the roentgen irradiation plays the essential rôle in the results obtained from the irradiation. This author substantiates the hypothesis which, however, still needs experimental proof, that the cholin liberated by the roentgen irradiation influences the process of conduction of stimuli at the synapse into the ganglia, therefore, at the point of transition of the preganglionic fibers into the ganglionic cell.

At present it cannot be stated whether this in-

fluence is of an inhibitory or accelerating type.

On the basis of the existing data, this author expresses the view that the autonomous nerve endings and the points of transition of the preganglionic fibers into the ganglionic fibers into the ganglion change their irritability probably as a result of a cholin or a cholin-like substance liberated through the irradiation and that these changes are centripetally conducted in the sense of an increased or decreased irritability and come to manifestation as distant effects in other regions supplied by the vegetative nervous system while at the point of application of the roentgen rays only the local radiation effects are demonstrable.—A. S. Schwartzman.

Wüst. Untersuchungen über den Wert des Röntgen-Schichtverfahrens für die Diagnostik des Hals-, Nasen- und Ohrenarztes. (Investigations concerning the value of the roentgen layer technique for the otorhinolaryngologist.) Fortschr. a. d. Geb. d. Röntgenstrahlen, June, 1939, 59, 509-551.

This is a long paper from the Charité in Berlin dealing with the experiences with the roentgen layer technique. The first part is concerned with a technical comparison of the two methods. One instrument is the planigraph, manufactured by Siemens according to the principle of Ziedses des Plantes, and the other the tomograph from the firm Sanitas. In the planigraph there is a sinus curve excursion of both the tube and the film while with the tomograph the motion is confined to the tube. It was found possible to cut a much thinner layer with the tomograph than with the planigraph; the planigraph, however, produced a more complete obliteration of the other layers. The method for studying skulls and sinuses is described and illustrated with particular attention to malignant tumors of the antra. If one may judge from the reproductions, the results are not impressive. One figure, however, shows an anteroposterior view of the larynx with the soft tissue detail brought out with great clarity.

One section deals with the comparative value of the conventional film, a film overexposed using the Potter-Bucky diaphragm, and the roentgen layer method in the study of the bronchial tree and especially for the identification of small foreign bodies of low density. The experiments were carried out on dogs and the

results seem to show a decided superiority of the layer technique. This also proved to be true in one clinical case where a bone fragment was lodged in a right main bronchus surrounded by dense lymph gland shadows.—W. A. Evans, Jr.

Birkelo, C. C., and Brosius, W. L. Roentgen visualization of pulmonary arterial circulation in autopsy material. *Radiology*, Sept., 1938, 31, 261-292.

A method of studying the vascular alteration in the lung as the result of disease is described. The thoracic contents were removed en masse, preserving the same degree of lung collapse that was present before death as shown by the ante-mortem roentgenograms. The pulmonary artery was severed at the pulmonary ring and the heart and aorta dissected free from the lung. Then radiopaque material was injected into the pulmonary artery under constant manometric control. Roentgenograms were made of the inflated lungs before and after injection. The lungs were then deflated and re-injected with a fixing solution and later sectioned.

This is a preliminary report of the method and early observation. At present it seems probable that pulmonary tuberculosis causes a marked decrease in pulmonary arterial circulation in the portion of the lung involved and that this impairment is proportionate to the degree and stage of the tuberculous involvement and that it is permanent. They found that collapse measures decrease the total volume of pulmonary arterial circulation in proportion to the degree of collapse, but the circulation returns to normal when the lung reexpands.

There are a number of excellent illustrations of this work.—J. H. Harris.

REINHARD, M. C. A note on the use of clinical dosage meters using a thimble ionization chamber. *Radiology*, 1939, 32, 282-283.

The author calls attention to: (1) The existence of a shadow cast when a thimble ionization chamber with a metal chamber tube is placed in the radiation beam either between the filter and the skin or directly on the skin. This shadow causes a definite decrease in the intensity of the roentgen-ray beam. (2) The variations in intensity when the thimble ionization chamber is placed in the center or at the periphery of the radiation area. The difference may amount to 20 per cent. (3) The variation in intensity with the degree of submergence of the chamber on the skin surface. This may amount to a difference of 12 per cent.—J. H. Harris.

BLAIR, HARRY C. The alternation of blood supply as a cause for normal calcification of bone. Surg., Gynec. & Obst., Oct., 1938, 67, 473-473.

The author attempts by a correlation of certain clinical observations and theoretical considerations, to present a rather reasonable theory that normal calcification of bone is maintaired by alternating ischemia and hyperemia. This same mechanism aids in the treatment of fracture. He feels that he has sufficient evidence to establish the idea that this variation in the blood flow to a given part of the skeleton is produced by the contraction and relaxation of muscles. The entire article must be read to appreciate the author's viewpoint for a short abstract cannot include all of the important theoretical considerations. However, it is important to bring out that if the theory is correct, then the clinical applications are very important, i.e. that heat and massage are contraindicated in recent fractures since they produce haperemia and thus abnormal mobilization of calcium from the bone. Heat should be used only to help absorb calcium as in the case of calcification in a bursa. On the other hand, coatrast baths and the use of alternating suction and pressure would be indicated. In fractures of the femoral neck, where because of the age of the patient the blood supply at best is poor, ischemia might actually help in the precipitation of bone salts if the other factors which send to produce the opposite effect could be eliramated. This calls for very rigid anatomica fixation, however. Further, fixation of the wrst in fractures of the navicular should theoretically be done without preventing the use of the hand in order to facilitate healing here.—P. C. Swenson.

MELTZER, H., and KÜHTZ, E. H. Über den Einfluss der Röntgenbestrahlung auf das anorganische Gewebegerüst der Haut. (The influence of roentgen irradiation on the inorganiz tissue framework of the skin.) Strahlentnerzpie, 1938, 62, 406–424.

An attempt was made by the authors to determine whether under the influence of roent-

gen irradiation of the healthy skin any changes in the irradiated region occur in the salt content of the inorganic tissue framework, what is the nature of these changes, how soon after the irradiation do they appear and what differences are observed following a single and following a fractional irradiation.

At first a series of preliminary experiments was carried out which revealed that no differences whatsoever could be demonstrated in black and albino normal rabbits following roentgen irradiation with 220, 825 and 1,100 r. In the microscopically stained preparation any significant irradiation effect was not demonstrable. On the other hand, the reaction to the irradiation was clear cut in the charred preparation. For further study irradiation with a dose of 220 r appeared to be sufficient.

A single roentgen irradiation of the skin of the back of rabbits with 825 r was found to produce regularly definite changes in the inorganic salt content of the irradiated skin region. The changes came to manifestation in the epithelial and in the connective tissue parts. An increased salt content is already demonstrable seven hours after the irradiation. It reaches its highest point about thirty-one hours after the irradiation after which it begins to decrease

during the following two to six days. After the seventh day, however, there regularly occurs an increase in the salt content which again reaches its highest point at about the twelfth day.

One has to deal here, therefore, with a biphasic reaction. It appears to be highly independent of clinical and histologic tinctorial parallel manifestations. The first phase of the salt increase corresponds somewhat to the early erythema and the second phase to the main erythema.

The increase and decrease does not affect all types of salts uniformly (reference is had to soluble and insoluble magnesium and phosphate salts). The relationship between the soluble salts and insoluble calcium salts apparently follows a given law during the course of the irradiation reaction. The authors believe that there is no other available method which would permit one to determine as exactly as the method under consideration the age of a roentgen reaction in the experiment.

Also following a fractional roentgen irradiation of the normal skin of rabbits with 825 r there is demonstrable a biphasic reaction but here the reaction is not as clear cut.—A. S. Schwartzman.



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## CORRELATION OF POSTMORTEM CHEST TELEROENT-GENOGRAMS WITH AUTOPSY FINDINGS

# WITH SPECIAL REFERENCE TO PULMONARY EMBOLISM AND INFARCTION\*

By AUBREY O. HAMPTON and BENJAMIN CASTLEMAN BOSTON, MASSACHUSEUTS

EXACT and detailed confirmation of the interpretations of roentgenograms of the chest is often difficult to obtain for three reasons: First and most important is the fact that, even if an autopsy is performed, one cannot rule out any change that may have occurred between the time of the last roentgenogram and that of death. There is no doubt that during the last few hours of a patient's life a large quantity of fluid may accumulate; bronchopneumonia can become more widespread; hemorrhage into a tumor can increase its size. Quite often correlations between roentgen and pathological findings are unjustly made with roentgenograms taken several days or even weeks before autopsy, despite the extensive changes which can occur during this period. Secondly, if an attempt is made to take roentgenograms shortly prior to death, it is necessary to use a portable machine and the roentgenograms may not show the lesions sharply and accurately. Finally, when the lungs are removed at postmortem they are collapsed, and accurate correlation between the air-distend-

ed lang as seen on the roentgenogram and the autopsy specimen is practically impossible. This is especially true as regards distances and locations of lesions. To obviate these difficulties and to leave no loophole for the sometimes undue skepticism on the part of roentgenologists for pathologists who do not find what the former have seen or discover what the roentgenologist has missed, a cooperative method was devised to study the chest.

#### METHOD

As soon as permission is granted for a postmortem examination a chest roentgenogram is taken of the body at a distance of 7 feet. The body is suspended vertically against a wall, upon which a plate holder is permanently fixed (Fig. 1). The method of suspending the body consists in using a very sturdy leather halter (canvas is not strong enough), the front part of which fits smagly under the chin, with side straps around the face and secured at the back of the neck. The halter is lined with felt so that the face is not marred. The halter and

<sup>\*</sup> From the Departments of Roentgenology and Pathology, Massachuserts General Hospital, Boston. Read at the Thirty-ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 20–23, 1938, and before the New England Pathological Society, Feb. 16, 1939.

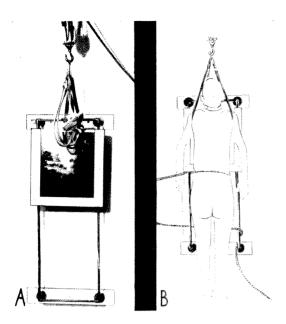


Fig. 1. A, the plate holder attached to wall, and leather halter attached to hook and pulley which is firmly bolted to ceiling; B, the body is suspended by halter and ropes.

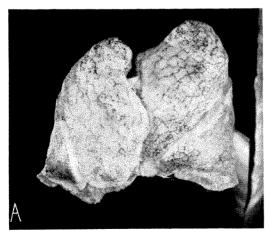
the ropes under the arms which give further support for the body are both attached to a pulley arrangement which is securely attached to the ceiling. Both posteroanterior and lateral roentgenograms are taken. A tube with a fine focus is used and 15 masec. of exposure is given for the posteroanterior view and 45 masec. for the lateral. In cases of suspected pneumothorax or

chest wall lesions the autopsy is not begun until the roentgenograms have been interpreted. Usually, however, no further delay in the autopsy is necessary.\* At autopsy both lungs are removed together with the trachea, great care being taken not to tear the visceral pleura. Kaiserling solution No. I (a formalin fixative) is instilled by gravity through the trachea until both lungs are approximately the same size as they were during life (Fig. 2). The trachea is then clamped and the specimen submerged in a large crock containing the same fixative and allowed to remain for about a week. At the end of this period the lungs are sectioned by the pathologist in the presence of the roentgenologist. An attempt is made to find anatomical explanation for all the shadows seen on the postmortem roentgenograms and conversely the roentgenologist attempts to see on the roentgenogram most of the lesions present in the specimen. We have studied 400 cases according to this method.

# THE NORMAL POSTMORTEM ROENTGENOGRAM

After death there is reduction in the size and incomplete aeration of the lung appar-

\* Obviously, this method insures having chest roentgenograms on patients who have been too ill, or who have died too soon after entry to have one taken. Occasionally this is important if an unusual or unsuspected chest lesion is discovered at autopsy.



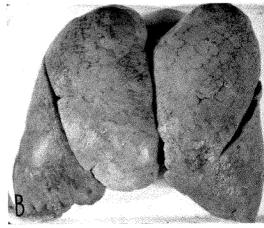
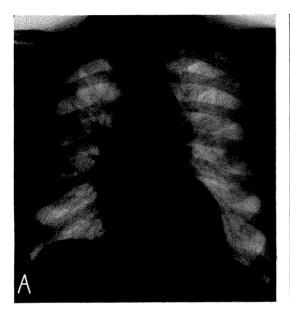


Fig. 2. Lungs before and after injection. Note the smaller size and ill defined character of the deflated and collapsed specimen, A, when compared with the inflated, sharply outlined injected lung, B.

ently due to narrowing of the intercostal spaces, the high position of the diaphragm, and the contraction of the lung because of its inherent elasticity. The usual postmortem roentgenogram of the chest at close distances with the patient horizontal has often been shown to be unsatisfactory because of incomplete aeration of the lungs and distortion. By suspending the body in the upright position in the manner already

in the posteroanterior diameter of the chest. A comparison of the antemortem and postmortem roentgenograms taken of a patient with normal lungs shows a marked variation in the heart and pulmonary vascular saadows. In the postmortem roentgenogram the blood vessels are usually much smaller and less distinct, the aorta about one-half the diameter, and the heart either dilated or contracted. The chief dif-



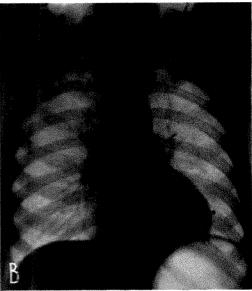


Fig. 3. A, antemortem roentgenogram of normal chest. 3, postmortem roentgenogram, same subject, position and technique. Note elevation of diaphragm and mediaction in size of aorta and pulmonary vessels.

described, however, this decreased aeration of the lung is somewhat compensated for by the downward traction of the diaphragm by the abdominal viscera, and by the widening of the intercostal spaces by means of the rope supports under the axillae. The general appearance of the postmortem roentgenogram of the chest corresponds to one taken antemortem during quiet breathing or expiration (Fig. 3). The diaphragm is usually about two interspaces higher than that seen on an inspiration roentgenogram, the upper lobes are fairly well expanded, and the lower lobes are incompletely aerated. The latter fact is particularly noticeable in the lateral view, which also shows a considerable reduction

ferences, therefore, in the antemortem and postmortem roentgenograms are the degree of aeration of the lung and the alteration in the size and shape of the cardiovascular shadows.

## PULMONARY EMBOLISM AND INFARCTION

Aithough there are many potential aspects of a correlative study of this type, in this report we shall deal only with the problem of pulmonary embolism and infarction. As the project advanced it became quickly apparent that many of the elementary features of pulmonary infarction were not understood adequately enough to permit of accurate correlation of roentgenograms,

clinical histories, and anatomic findings, and an extensive anatomic and histologic study proved necessary to provide an adequate background. For this purpose use was made of a larger series of cases drawn from the 3,500 autopsies performed in the laboratory during the ten year period before the combined study was begun. In this larger series either pulmonary embolism or infarction was noted in 9 per cent of the cases, and in 3.5 per cent of this same group it was considered a major cause of death. In the combined study group of 400 cases in which unquestionably a more careful examination of the lungs was made, 14 per cent of the cases showed either pulmonary embolism or infarction—an apparent increase of over 50 per cent.

Classical teaching, as recorded with little variation in the textbooks of two generations, has told us that pulmonary embolism may or may not be accompanied by infarction of the lung. The accepted explanation based on experiment and clinicopathologic correlations of human material is that embolism to a lung with an otherwise normal circulation never produces infarction, whereas an embolus to a lung with a previously impaired circulation, usually by chronic passive congestion, regularly does produce an infarct. Though true in a general way, many exceptions will be met in any series of routine autopsies, many more we believe than is generally recognized. Pertinent figures will be found in the succeeding pages. Moreover, between the two simple categories of embolism without and embolism with infarction we believe a third hitherto unrecognized group of clinical importance must be inserted, embolism with incipient but abortive infarct-like reaction of the pulmonary parenchyma, a group which we have described as incomplete in-

In analyzing all of our cases with embolism and infarction—a total of 370 cases—it was found that only 40 per cent were post-operative patients and that of the remaining 60 per cent only half were cardiac patients. In other words, 30 per cent of the

cases were noncardiac medical patients, a group in which one does not usually appreciate the danger of pulmonary embolism or infarction.

### TABLE I

## STATISTICAL DATA ON 370 CASES OF PULMONARY EMBOLISM AND INFARCTION

Postoperative 40% of which 58% had infarcts Cardiac 30% of which 90% had infarcts Noncardiac medical 30% of which 62% had infarcts

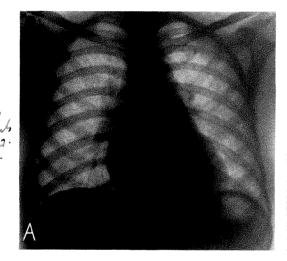
In a routine autopsy the sources of emboli are usually not searched for too carefully or industriously. Very often restrictions do not permit examination of the extremities. We have observed that a very large percentage of the emboli arise from symptomless thromboses of the deep veins of the legs, usually in the popliteal region. These findings confirm those reported by Rössle, who examined the deep veins of the legs in 400 consecutive autopsies and found thromboses in 27 per cent of the cases over 20 years of age. Of course, in many of the cardiac cases, especially those with rheumatic heart disease and auricular fibrillation, the emboli arise from right auricular mural thrombi. However, even in some of these cases the deep leg veins are also thrombosed.

# PULMONARY EMBOLISM WITHOUT INFARCTION

The gross pathology of any organ, and especially the lung, is, of course, the important feature to the roentgenologist, and for the sake of completeness we will review some of the elementary facts. Pulmonary embolism may involve the main branches alone, producing as a rule sudden death, or it may involve some of the terminal branches and be completely asymptomatic. Roentgenograms of acute fatal pulmonary embolism show no definite variation from the normal, but those patients surviving massive embolism may show an acute pleural effusion. Massive pulmonary embolism can occur in either or both main vessels . with subsequent organization and superimposed thrombotic extension producing a cor pulmonale. Without a definite history

of an embolic attack, it would be almost impossible to differentiate this condition from a localized thrombosis of the pulmonary vessels. In either of these two conditions the gross pathology consists of dilated pulmonary vessels completely occluded by laminated thrombi. This lesion may exist for years and, because of the very gradually diminishing lumen, enough of a collateral circulation, especially with the bronchial arteries, may be established to

ing right-sided heart enlargement (cor pulmorate) and dilatation of the hilar vessels. Further evidence for a diagnosis of pulmonary thrombosis was a definite right axis devation on the electrocardiogram. The patient died very suddenly five weeks later. Figure 4B is a photograph of the autopsy specimen showing almost complete occlusior of both main pulmonary arteries by old organized thrombus. It is quite likely that the alleged pneumonic episodes were



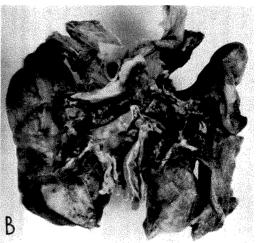


Fig. 4. A, case of chronic pulmonary thrombosis. Note enlargement of right heart and hilar vessels. B, gross specimen of same case, showing the old organized thrombosis of the main pulmonary arteries.

prevent infarction.<sup>2</sup> It is of further interest that such lesions very often cause only minimal symptoms. Fragments of this large thrombus, however, may break off and extend farther down the pulmonary tree to produce infarcts.

A case\* that exemplifies this condition very well is that of Negress, aged thirty-five, who entered the Massachusetts General Hospital complaining of cough and dyspnea. One and a half years and one year before admission she supposedly had pneumonia associated with fever, cough and rusty sputum. The fever subsided, but the cough continued and was soon accompanied by dyspnea. Figure 4A is a roentgenogram taken soon after this admission show-

attacks of pulmonary embolism from which the pament recovered and that secondary thrombosis developed.

## COMPLETE INFARCTION

Size. Infarcts vary in size from 0.3 to 10 cm., the average being about 3 by 2 by 1 cm., and there are usually several in each lung. A small portion of the margin of the lobe may be involved and such lesions are often no more than 1 cm. in thickness. Such small peripherally placed lesions produce mentgen shadows that have more the appearance of localized pleural thicken ng than of areas of consolidation.

Location. Infarcts are always peripheral in location, i.e., one or more pleural surfaces are invariably involved. Usually these lesions occur at the junction of two or more pleural surfaces, such as at the costophren-

R.

<sup>\*</sup> This case was reported in detail in the Case Records of the Massachusetts General Hospital, Case 22471, New England J. Med., 1936, 215, 982-985.

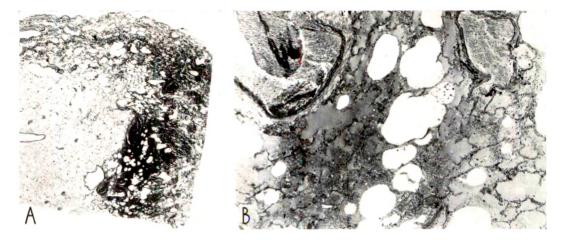


Fig. 5. A, photomicrograph of an infarct one day old. Note the absence of a sharp line of demarcation and the presence of air in the atria and alveolar sacs. B, higher power photomicrograph showing intact alveolar walls and edema and hemorrhage within the alveoli.

ic angles, at the anterior and posterior lung margins near the mediastinum, or at the margins of the middle lobe. An infarct in the latter location or in a costophrenic angle is very common because the lung is thin and the infarct would be almost completely surrounded by pleura. The distribution of infarcts in our series corresponds fairly well with that recorded in the literature. Seventy-four per cent of them were located in the lower lobes, 43 per cent in the right and 31 per cent in the left. The remainder were distributed almost equally among the other three lobes.

Microscopic Pathology. During the first

day and probably the second day of infarction, there is no definite destruction of alveolar walls. There is merely a very marked congestion of the capillaries and diapedesis of the red blood cells into the dilated alveoli of the region involved. The word "infarct" is derived from "infarcire," meaning to stuff, and aptly fits this stage of its development. During the first few days only the alveoli, the smallest air-containing unit in the lung, may be filled with blood, while the larger units, such as the alveolar sacs and atria, may still remain aerated. This accounts for the fact that an infarct in this early stage is not uniformly solid grossly

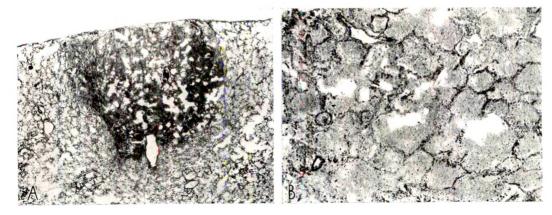


Fig. 6. A, photomicrograph of an infarct about four days old. Note its peripheral location, the beginning of encapsulation, and the presence of air in the alveolar sacs and atria. B, a higher power showing definite destruction of alveolar walls and more cellular infiltration.

and why its corresponding roentgen shadow may be so difficult to visualize. The roentgen shadow of an early infarct does not usually develop before twelve hours and occasionally not before twenty-four hours after onset of symptoms. During this stage the infarct is often not sharply defined and may simulate focal hemorrhage or bronchopneumonia (Fig. 5).

thrombus or embolus." Because of the onset of the process of organization which usually begins during the second week, the infarct changes from the bright red to the dark or black-red color, becomes more solid more sharply defined and in time even smaller in size (Fig. 6). Depending upon the size of the infarct, organization may last for weeks to months. The granulation tis-

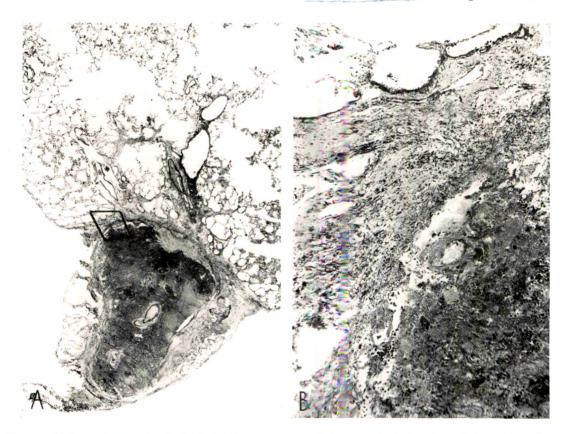


Fig. 7. A, photomicrograph of a healing infarct. Note the shart and thick capsule and the organized and recanalized thrombus in a vessel just proximal to the infarct. E, a higher power through the blocked area in A showing the thick granulation tissue of the capsule and accillular necrosis within the infarct.

After the second day there is beginning necrosis of the alveolar walls and degeneration of the red blood cells. As this process continues there is dehemoglobinization of the red blood cells, and the appearance of hemosiderin-laden phagocytes and occasionally hematoidin crystals. This stage is in keeping with the usual dictionary definition of the word "infarct"—"necrosis and hemorrhage in an organ, resulting from obstruction of the local circulation by a

sue appears initially at the periphery of the infarct and slowly migrates inward. This marginal organization produces a pseudocapsule which explains the sharp outline and the gradual shrinkage in size of the older infarcts (Fig. 7). A small infarct will become a fibrous scar much sooner than a very large one, the latter often remaining hemorrhagic indefinitely.

Shape. An infarct is sharp in outline and the roentgen shadow cast by it will also be



Fig. 8. Low power photomicrograph of an infarct in a costophrenic showing the "hump"-shaped convexity of its proximal edge.

sharp if the infarct is projected through its greatest thickness. For example, an infarct involving most of a lower lobe will be sharp in outline in the lateral view but indistinct in its upper margin in the posteroanterior view. The shape of the infarct is dependent entirely upon the shape of the part of the lung it involves. Since infarcts are always in contact with visceral pleural surfaces it can readily be seen that these pleural surfaces will form at least one side and more commonly two or three sides of the infarct; thus, to this extent the shape of the lesion must correspond to the shape of the lung involved, and this varies. If the lung tip which fits into the costophrenic angle is infarcted the consolidation may extend for varying distances from the periphery inward toward the heart depending, of course, upon the size of the vessel in which

the embolus lodges. Similarly, if a part of the lingula of the left upper lobe or the middle lobe of the right lung is involved, the consolidation extends to the pleural surface or surfaces. If the whole lingula or the whole middle lobe is infarcted, the infarct will of course be the shape of these structures. The long axis of the infarct is always parallel to the longest pleural surface involved. The length and extent of the pleural surfaces involved may vary markedly. For example, the entire lateral and inferior margin of the middle lobe may be involved, producing a long narrow area of consolidation. It is important to note that the cardiac margin of such a lesion has the same general characteristics of a large, more rounded infarct. The medial or cardiac margin of an infarct is convex toward the heart, presents a serrated margin, and, if the central roentgen ray is tangent to it, a a convex, slightly irregular "hump"-shaped shadow is produced. When the lateral costophrenic margins of the lung are involved, the posteroanterior view of the chest shows the "hump"-shaped shadow. When the anterior and posterior costophrenic margins are involved, the "hump" shadow is seen only in the lateral view. Since infarcts may involve any peripheral portion of the lung, including the surfaces of the interlobar fissures, it is often advisable to obtain both oblique and lateral views of the chest before an accurate differentiation can be made between areas of consolidation due to infarction and some other pathology.

While it is true that shadows of infarcts may be roughly triangular in the postero-anterior view of the chest, they are rarely if ever actually triangular in shape. If one studies the margins of the lobes of the lung in their inflated state it can be seen that where two pleural surfaces meet, two sides of a triangle may be formed, but these surfaces are in contact with the chest wall except along the interlobar pleura and therefore the two sides of the triangle formed are not visible, i.e., there is no contrast between the infarct and the chest wall at the points where the triangular shadow is more read-

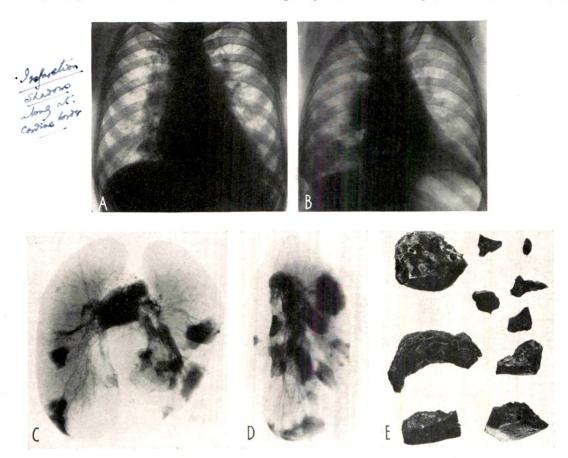


Fig. 9. A, patient with rheumatic heart disease, early infercts at both costophrenic angles and along the right border of the heart, B, same subject postmortem, sincen days later. There are now nine infarcts in the right lung and five in the left, those on the left being partially obstructed by the heart shadow. The triangular densities on the right are due to summation of several infarcts, the interlobar fissure contributing to make a total shadow. The right lung root is partially obscured by a large infarct at the anterior margin of the right upper lobe. C and D, the lungs of B have been removed, injected and fixed with formalin, then inflated and partially dried. The infarcts can be seen more clearly and their true shapes determined. The largest area of density, in the center, represents the infarct in the anterior margin of the right upper lobe. Although the shadows appear triangular in shape in the anterioposterior view, in the lateral view (D) they are not at all triangular. The most pointed margin (apex) is directed away from the heart; i.e., to the pleural surfaces. Note that the cardiac margins of all the infarcts are convex instead of pointed. The lesions correspond in shape to the pleural surfaces involved. E, ten of the infarcts have been dissected away from the surrounding lung and the irregular shape of the lesions can be better appreciated.

ily visualized. The textbook description of infarcts leads one to believe that they are pyramidal in shape with their apices pointing toward the heart, but this is not true even in instances where a roughly pyramidal or triangular shadow occurs. The apex of the triangle or pyramid is directed away from the heart instead of toward it. The cardiac margin of the infarct is rounded or "hump"-shaped instead of pointed. Figure 8 shows a cross section through an

infarct in a costophrenic angle showing the convex "hump" shape at its cardiac border and the sharp apex peripherally.

The size, shape and location of the common infarcts in the lung are well illustrated in Figure 9. Figure 9.1 is an antemortem roentgenogram showing indefinite areas of density along the right margin of the neart and at both costophrenic angles. These shadows represent early infarction but a positive diagnosis could not be made

from this examination alone. Figure 9B is a postmortem roentgenogram taken sixteen days later, now showing fourteen separate infarcts in the lung, nine on the right side and five on the left. The largest single infarct occupies the medial anterior margin

ize better and demarcate accurately the shape of the infarcts in this case, the lungs were removed at postmortem, fixed in the routine manner by injecting formalin through the trachea, and then dried by blowing air through the trachea for about

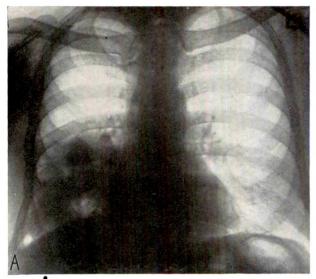






Fig. 10. A, multiple infarcts in an ambulatory patient with phlebitis of sixteen years' duration. Chief complaint—dyspnea on exertion. No pain or blood spitting. B, right lateral view shows multiple, sharply defined areas of consolidation involving the right upper, middle and lower lobes. C, spot film right lung taken in oblique position during roentgenoscopy. Irregular rounded mass simulating tumor but it is obviously composed of multiple sharply defined areas of consolidation. Note the convex cardiac margin of an infarct in the right upper lobe.

of the right upper lobe. The lower lateral margin of the upper lobe, the lateral margin of the middle lobe and the lower lateral margin of the left lower lobe also show large infarcts. The triangular shapes of the largest areas of density in the right lung are due to summation of the shadows of several infarcts, the interlobar fissure contributing to make the total shadow. In order to visual-

twenty-four hours under a pressure high enough to keep the lungs distended without forming artificial blebs or rupturing alveoli. Roentgenograms of this specimen (Fig. 9C and D) show much more clearly the exact shape of the infarcts because the parenchyma adjacent to them is very well aerated. The largest area of density in the center represents the infarct of the anterior

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nargin of the right upper lobe somewhat distorted. This lesion corresponds to the shape of this portion of the lung as do all the other infarcts seen. The medial or cardiac margins of all the infarcts are irregular and convex in shape. The only infarct in the whole group which is truly triangular occupies the right costophrenic angle but the apex of the triangle is directed downward and this triangular shape is not visible on the roentgenograms because there is no contrast between the area of consolidation, the diaphragm and the chest wall. Similar infarcts are seen more clearly in Figures 12 and 16. In summary, it should be noted that none of the infarcts illustrated in Figures 9A, B, C and D, are actually pointed toward the heart shadow, that they are not pyramidal in shape, that they are not truly triangular, but that all of them correspond in shape to the portion of the lung they involve and are convex toward the heart shadow. In Figure 9E, which shows ten of the infarcts dissected out from the lungs, the irregular shape of the lesions can be better appreciated. Plaster-of-Paris models were made of these infarcts and by the study of these, the characteristics already mentioned are even more obvious.

When more than one infarct occurs in the same lung, and especially when they are closely placed, the sharply defined shadows which vary in shape can be projected so as to produce a summation shadow of nearly any shape. It is therefore very important to attempt to separate the shadows into their component parts and to determine the location, size and shape of these parts. In other words, a "dissection" of a conglomerate shadow for differential diagnosis can be done only by roentgenoscopy and by the taking of roentgenograms in different positions. An example of this aspect of the shape problem is well illustrated in the roentgenograms (Fig. 10) of a fifty-six year old physician who had a history of phlebitis in both legs of sixteen years' duration and who developed pain in the right chest following ligation of several of these veins. The conglomerate dense

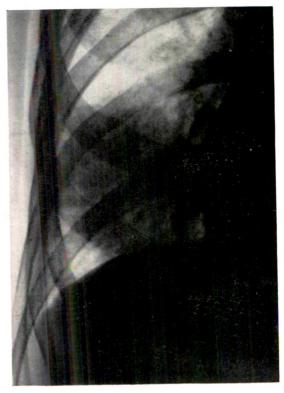


Fig. 11. Postmortem roentgenogram showing two infarcts measuring 5 by 5 by 4 cm. and 3 by 3 by 2 cm., producing, when superimposed in the posteroanteric view, a rounded shadow.

shadows on the right side in Figure 10A are seen in the lateral view (Fig. 10B) to be composed of sharply defined areas of consolidation arranged along the periphery of the right lower, right upper and middle lobes. They are convex toward the heart shadow, end sharply at the interlobar pleura and the intervening lung is well aerated. In the oblique view taken during roentgenoscopy (Fig. 10C), an irregularly rounded shadow is seen, simulating a tumor, but or closer examination it is obviously made up of multiple discrete shadows. The upper margin of the rounded shadow shows the irregular convexity toward the heart, previously described. The lower margin of this shadow ends at a horizontal line corresponding to the base of the right upper lobe. The lower portion of the rounded shadow corresponds to infarction in the middle lobe. During roentgenoscopy the exact location and size of the lesions

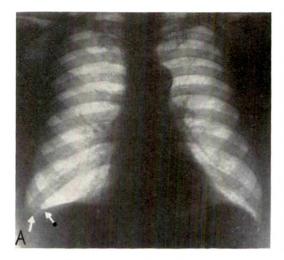
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could be easily determined. They could be seen to move freely with respiration. The heart shifted to the right on inspiration. A roentgenogram seven months later shows disappearance of the large shadows leaving only dense thin lines.

Round shadows, which one does not usually associate with infarction, may be produced by two or more infarcts if projected in the proper direction. This is seen fairly

Differential Diagnosis. Too often the diagnosis of pulmonary infarction is made only when the clinical symptoms suggest it; i.e., when the patient has chest pain, blood spitting, and shows on examination a pleural friction rub and phlebitis. From our experience, it is quite evident that very often only one symptom and occasionally none is present when an infarct is quite obvious on the roentgenogram. The frequent



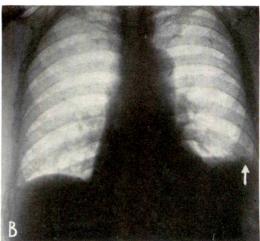




Fig. 12. A, small infarct, right costophrenic angle. See text for history. C, spot film, right costophrenic angle, showing small area of density with "hump"-shaped upper margin occupying costophrenic angle. B, same patient seven days after first examination with infarct at left base. Note the convex upper margin of density near the costophrenic angle and unusually high position of the left side of the diaphragm.

well in Figure 10C in the case described above and a better example is illustrated in Figure 11, a postmortem roentgenogram, which shows a rounded shadow at the right base on the routine posteroanterior view. This shadow in the lateral view is not round but is composed of two infarcts which at autopsy measured 5 by 5 by 4 cm. and 3 by 3 by 2 cm. Although there was aerated lung between the two infarcts, they were so situated, one on the diaphragmatic surface and the other on the anterolateral aspect, that they formed a round roentgen shadow in the posteroanterior view.

unwillingness of clinicians to accept a roentgenologic diagnosis of infarct is well illustrated in the case of a man, aged fifty-two, who had a sudden severe right chest pain which lasted for eight hours and which required morphine for relief. One week after the acute attack a roentgenogram (Fig. 12 A and C) showed a rounded shadow at the right costophrenic angle. The roentgenologic diagnosis of infarction was not accepted because there was no history of blood spitting and no clinical evidence of phlebitis. The patient was allowed to proceed about his business until one week

ater, when a similar sudden severe pain occurred in the left chest. Another roentgenogram (Fig. 12B) showed a similar lesion in the left costophrenic angle. At this time a nedical consultant discovered signs of phlebitis in the left popliteal vein and upon more careful questioning elicited a definite history of blood spitting. The patient was kept in bed for two weeks and no further symptoms have developed for over a year.

Most of the clinical signs and symptoms of an infarct are also present in carcinoma of the lung. It is therefore quite important to be able to differentiate the two conditions. In this series there have been 3 cases of pulmonary infarction diagnosed erroneously as cancer, due almost wholly to the fact that an inadequate examination was made. Figure 13 is an antemortem roentgenogram of a patient who was in the hospital several years before this study was begun and whose clinical history was consistent with cancer of the lung. The roentgenogram was interpreted as being consistent with cancer; an infarct was not even considered. The patient died a short time

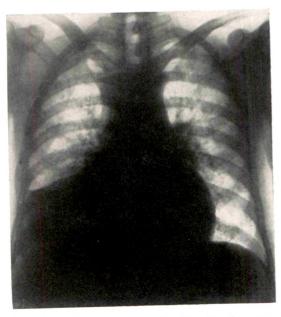


Fig. 13. Antemortem examination showing complete consolidation of the right middle and lower lobes, simulating cancer. At postmortem shadows were due to almost complete infarction of middle and lower lobes.

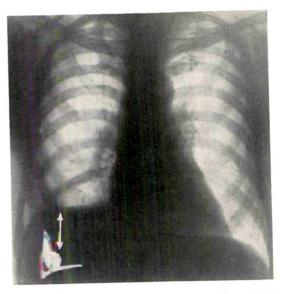


Fig. 14. Examination twenty hours before death. Infarcts at right base at autopsy: (1) posterior costophrenic angle, measuring 8 by 3 by 9 cm.; (2) anterior inferior margin of the lower lobe near the middle lobe septum, measuring 4 by 3 by 1 cm.; and (3) anterior costophrenic angle, measuring 2 by 1 by 1 cm.; 150 cc. of fluid.

later and at autopsy there was complete infarction of the right middle lobe and the greater portion of the right lower. Certainly the displacement of the heart and mediastinum to the right, the large thickened lung roots and the evidence of reduction in size of the middle and lower lobes suggest malignant disease. It might have been possible, however, to demonstrate small portions of aerated lung between the large infarcts if over-penetrated Potter-Bucky diaphragm roentgenograms had been taken. If normally aerated lung can be demon-) strated between multiple, sharply defined, peripherally placed areas of consolidation involving one or more lobes, it follows that the bronchus to the lobe or lobes cannot be obstructed because in bronchial obstruction all of the area supplied by the bronchus should present the same general density. As has already been stated, infarcts reduce the size of the lung, and in this manner may simulate collapse of the lung.

Another example of a case of pulmonary infarction diagnosed erroneously as cancer before admission to the hospital is that of a

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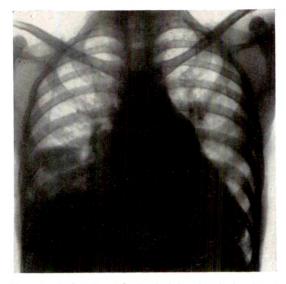


Fig. 15. Infarction of middle lobe simulating interlobar fluid or atelectasis. At postmortem forty days later lesion showed very little change in size or shape.

man, aged sixty, who had pleural pain and blood spitting for five days. There was a slight ecchymosis on the medial aspect of the left knee near a varicose vein. There were no other varicosities and the patient gave no history of injury, pain or discomfort about the knee. The diagnosis of pulmonary infarction was made from the hospital roentgen examination (Fig. 14) but was not accepted by the family physician who proceeded to give the patient exercises for testing his cardiac reserve. About ten minutes after these exercises the patient had an acute pulmonary embolism and died in an hour. Postmortem examination showed that the embolus originated in the left popliteal vein. There were three infarcts in the right lung and 150 cc. of fluid in the right pleural space.

When an infarct involves the right middle lobe, a not uncommon location as has been pointed out in the discussion of the shape of infarcts, the roentgen shadow may be mistaken for atelectasis or interlobar extension of pleural fluid. Figure 15 illustrates just this point. The shadow in the right middle lobe area is sharp in outline, convex inferiorly, and horizontal superiorly, corresponding to the shape of the lateral portion of the middle lobe. It does not extend to the lung root or axillary line. The absence of a fusiform shape differentiates the shadow from pleural effusion. The position of the shadow plus the fact that it does not extend to the lung root differentiates it from middle lobe atelectasis.

That pleural pain may be mistaken for breast pain is well exemplified in the case of a woman who complained of pain in the region of her right breast. Physical examination showed an angioma in this breast. This was removed and twelve days postoperatively she died of an acute massive pulmonary embolism. A roentgenogram (Fig. 16) taken very soon after operation and after another attack of chest pain in the same region as that previously experienced shows a sharp convex "hump"-shaped shadow at the right costophrenic angle quite characteristic of an infarct and another at the inferior margin of the middle lobe. Postmortem examination showed, in addition to the acute embolism, an organizing, definitely old thrombus partially oc-

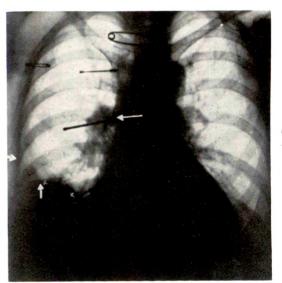
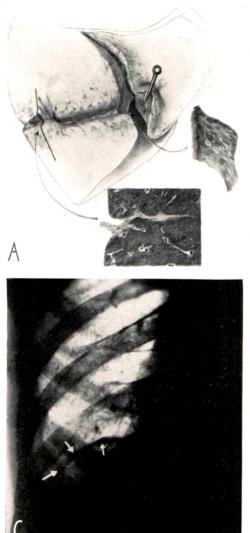


Fig. 16. Area of density in the right costophrenic angle with sharply defined, convex, "hump"-shaped upper border due to infarction. Enlarged right lung root due to chronic thrombosis of the pulmonary artery. Another small infarct is seen at the inferior margin of the right middle lobe, partially obscured by the diaphragm.



cluding a small pulmonary artery leading to a healing infarct at the right base and another more recent one in the middle lobe. There is no doubt that the pain in this case was due to the infarcts, and had a roentgenogram of the chest been taken preopning as an acute hemorrhagic lesion, passing through a healing stage, when it becomes smaller, sharper, dense, but maintaining its general shape, and finally ending as an organized healed scar.

Granted that small pulmonary infarcts



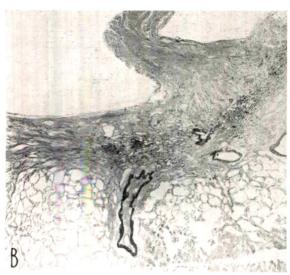


Fig. 17. A, healed infarct. Drawing of the right lung showing horizontal fibrous pseudoseptum across lower lobe. (1) The lower cross section drawing shows fibrous band extending from pleural tab into lung. (2) Cross section on right is from a healing infarct at medial aspect of lower lobe. B, photomicrograph through pleural tab showing the marked fibrosis in the healed infarct. Note the organized and canalized vessel just proximal to the infarct. An elastic tissue stain demonstrated elastic fibrils throughout this lesion. C, mentgenogram a short time prior to death showing the linear shadow which corresponds to the gross pathological specimen. Arrow points to retraction of the pleural margin opposite the dense line.

eratively and a diagnosis of infarct been made, the outcome might have been different.

## HEALED INFARCTS AND PLEURITIS

In describing the microscopic pathology of an infarct, we have shown that an infarct usually undergoes a definite cycle, beginare not uncommon and that many of them heal, it should be possible to find them at autopsy in their healed stage. It seems improbable that pathologists have systematically searched for the healed infarcts in the past, or possessed any adequate criteria for recognizing them, and consequently the incidence of their occurrence is not known.

This is due to the fact that the usual method of examining the lungs in their fresh deflated state does not permit accurate observations of old scars, pseudosepta, and small linear areas of fibrosis. Our method of examination of the inflated lung with the aid of roentgenograms has made it possible to find these lesions grossly. Once having been demonstrated, they can then be removed for microscopic examination. If the microscopic section shows an old thrombosed or recanalized vessel, we can hypothesize that the lesion may have been an infarct in the past. We have been fortunate in finding a few such cases, in which there was a fairly definite history of an infarct months or years before death.

A good example of a case\* showing healed infarction is that of a man, aged sixty-two, who six months before his first entry to the hospital had what was called pneumonia which was followed a few months later by dyspnea and wine-colored pleural fluid. A roentgenogram at the first entry showed fluid at the right base with interlobar extension. A definite parenchymal lesion could not be visualized because of the superimposed fluid. The patient died five months later, about one year after the onset of symptoms. The autopsy showed a linear fibrous band (Fig. 17A) running completely across the right lower lobe forming an almost complete septum between the lower and middle thirds. The pleura was thickened over this pseudoseptum and in one place had formed a fibrous tab which was adherent to the parietal pleura. A microscopic section (Fig. 17B) across this zone shows masses of closely packed, tangled elastic fibrils—undoubtedly remnants of the original alveolar walls. Two lesions could produce such an end-result, an organized pneumonitis or a healed infarct. In favor of the latter was the finding a short distance toward the hilum from the zone of scarring of a large pulmonary artery which was completely occluded, except for small canalizing vessels, by an organized thrombus. The occluded portion of the artery lay within normal lung tissue, a fact which would be most unlikely if the thrombosis had been secondary to a pneumonitis. We feel confident, therefore, that this lesion was an infarct associated with pleural effusion at the first admission and that it healed completely producing the fibrous band and pleural thickening observed at autopsy. From the drawing of this healed infarct (Fig. 17A) it is easy to understand how this lesion could produce a linear horizontal shadow on the roentgenogram.† Figure 17C taken a short time before the patient's death still shows some fluid at the right costophrenic angle. The dense oblique line at the right base corresponds to the fibrous band seen in the drawing of the specimen. The retraction of the pleural margin opposite the dense line is visible (see arrow on figure).

Since an infarct of the lung is always peripheral and extends to the visceral pleura, it frequently stimulates a pleural reaction which is believed to be the cause of the pain in this condition. This reaction may or may not give rise to an effusion. In our series of infarcts pleural effusion was present in only 40 per cent of the cases, but in only onethird of this group, or in approximately 13 per cent of the whole group of infarcts, could a causal relation be inferred between infarction and the occurrence of pleural fluid. The fluid in the other cases was more likely due to congestive heart failure or was present on the side that did not have the infarct. Why some infarcts stimulate a serous reaction and others do not is still unsettled. We do not believe that the presence of infection is the provoking agent because secondary infection of an already existing bland infarct is extremely rare. Many infarcts, and especially those that are associated with fluid, will produce pleural thickening when they heal and we believe that if a more careful search is made by both roentgenologist and pathologist, evi-

<sup>\*</sup> This case was reported in the Case Records of the Massachusetts General Hospital, Case 24381, New England J. Med., 1938, 219, 438-443.

<sup>†</sup> The differential diagnosis of linear shadows of the lung will be discussed more fully in a later paper.

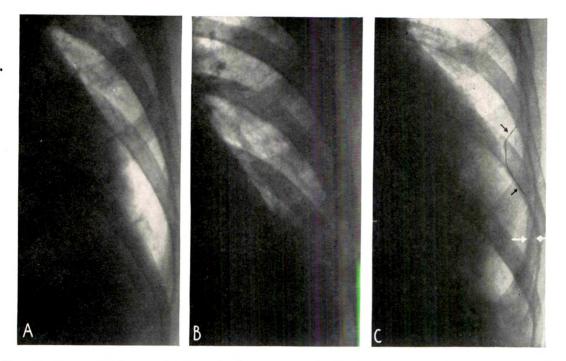


Fig. 18. A, normal left costophrenic angle. B, symptoms of infarct eight days before; 400 cc. clear fluid. C, same patient, one and a half years later. Note the thickened pleura and nodular shadow (retouched).

dence of infarction will be more often discovered as a cause of pleurisy.

While we do not wish to propose that all localized areas of pleuritis, peripheral scars, and anomalous septa are healed infarcts, there certainly appears to be a discrepancy between the very large number of clinical cases of sudden painful pleurisy, many associated with effusion and blood spitting, and the relatively rare pathological diagnosis of healed infarct. This is in part due to the fact that a localized pleuritis is usually assumed to be tuberculous in origin. We believe that if there is no evidence of active tuberculosis in the lungs, and excluding apical adhesions, the presence of a "dry" pleuritis or pleuritis with a sterile effusion is more likely to be due to infarction than tuberculosis. As has already been stated, the absence of a history of phlebitis, surgical operation, or heart disease does not rule out the diagnosis of infarction. If pleurisy with effusion is preceded or followed by a roentgen shadow simulating an infarct, the diagnosis is almost certainly established. Figure 18 illustrates this cycle. The

first roentgenogram shows a normal left costophrenic angle in a routine study of a patient with bronchial asthma. The second roentgenogram on the same patient taken eleven days later and eight days after an attack of left chest pain radiating to the shoulder and blood-tinged sputum shows left pleural effusion. Four hundred cubic centimeters of straw-colored fluid were removed. The patient died one and a half years later of coronary thrombosis. The third coentgenogram taken three weeks before death shows chronic pleuritis over the left lower lobe, more marked in the region of the healed infarct at the costophrenic angle and no pleural fluid. These findings were confirmed at autopsy.

# NCOMPLETE INFARCTION

Most carricians and roentgenologists are familia: with the postpartum or postoperative patient who suddenly on about the tenth to fourteenth day develops a little fever, spits up blood, may even have chest pain, and whose roentgenogram shows an infarct-like shadow (Fig. 19A). The symp-

toms usually last one to two days and the roentgen shadow disappears completely in two to four days (Fig. 19B). This roentgen shadow is usually interpreted as representing pneumonia or an infarct in spite of the fact that, although it is generally believed that infarction cannot occur in a normal lung, there is no evidence of pulmonary congestion or any other abnormal condi-

drome occurs not infrequently in the ambulatory patient without any indication of a source for an embolus and is sometimes incorrectly diagnosed as tuberculosis.

In 1922 Cutler and Hunt<sup>3</sup> described this clinical and roentgenological syndrome in postoperative patients and stated that the lesions were produced by small emboli arising from thrombi in the operative field.

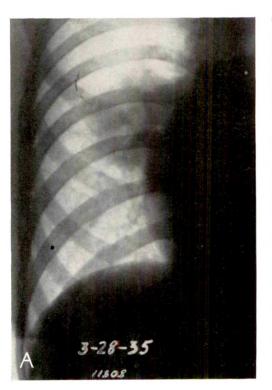




Fig. 19. A, incomplete infarct at right border of heart; B, same patient two days later. The lesion has disappeared.

tion. Since most of these patients get well, pathological confirmation of these interpretations has not been made. If this lesion were a true infarct with alveolar wall destruction, it could not disappear in a few days. It would have to heal and organize in the usual way, which has been described above, a process that would take more than a few days. One must infer, therefore, that the lesion did not involve the alveolar walls and that resolution of the process occurred. We have termed this lesion an incomplete infarct, one which terminates by resolution instead of by organization. This same syn-

They predicted, probably correctly, that pathologists would be loath to accept these lesions as infarcts. This hesitance may be attributed in part to the questionable relationship between lesions observed clinically in nonfatal cases and those observed both clinically and pathologically in individuals dying of another disease. In addition, although lesions produced by animal experimentations are not always analogous with those occurring spontaneously in man, experimental results in this condition would have been very difficult to evaluate without accurate knowledge of the exact

morbid anatomy of the human lesion. Practically all the experimental work on pulmonary embolism has shown that a true infarct cannot be produced in a normal lung, i.e., if we accept alveolar wall destruction as the necessary factor in the definition of the word infarct. If, however, pulmonary congestion was produced in the animals before the emboli were introduced, true infarcts developed. Recently Bardin<sup>4</sup> of the University of Paris and Steinberg and Mundy<sup>5</sup> in this country have presented evidence of the production of true infarcts in apparently normal dogs. They both feel that the reason why others have not been able to get comparable results is that they have not used a sufficient number of emboli to produce complete local circulatory obstruction. They neglect the fact, however, that when the pulmonary arteries are loaded with large numbers of emboli experimentally, the circulation is so embarrassed that the lungs are no longer normal. Most of the workers, however, including Cohnheim and Litten,6 Litten,7 and Karsner and Ash,8 did produce lesions in the normal lungs of animals, but because there was no alveolar wall destruction, they apparently ignored their findings. There was, however, edema, red blood

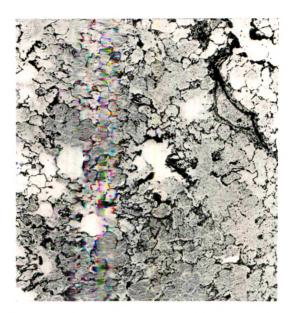
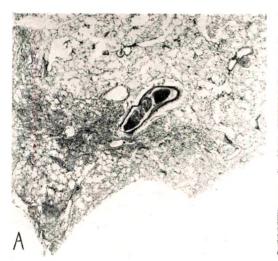


Fig. 20. Photomicrograph of an incomplete infarct produced experimentally in a normal dog. Note the intact alreolar walls and the hemorrhage within the alveolar.

cells and a few leukocytes in the alveoli. We repeated these experiments and produced similar lesions\* (Fig. 20). We believe that these experimental lesions produced in normal dogs correspond to what we have termed an incomplete infarct in

\* We wish to thank Dr. John D. Stewart of the Department of Surgery for his help with the animal experiments.



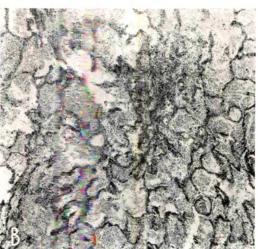


Fig. 21. A, low power photomicrograph of an incomplete infarct in a patient who died of acute massive embolism following a pelvic operation. Note the embolus just proximal to the lesion. B, a higher power showing intact alveolar walls and hemorrhage and leukocytes within the alveoli.

man. This clinical application of these positive experimental findings, which were previously interpreted as negative results, has not, so far as we know, been made heretofore.

Figure 21 demonstrates an incomplete infarct in a section from the right lower lobe of a woman, aged forty-three, who died of acute massive pulmonary embolism nine days following an operation for uterine suspension. She had complained of a rather indefinite slight right chest pain a few days before her death, but it was so vague that no roentgenograms were taken. The histologic appearance of this infarct is very similar to the lesion produced in the normal lung of a dog, as illustrated above. There is no alveolar wall destruction, merely edema and cellular deposits within the alveoli. The clinical importance of recognizing these disappearing shadows on the roentgenograms, of interpreting them as embolic in origin rather than pneumonic or infectious, and of repeated examinations, cannot be overemphasized, since it may be the only warning signal of a fatal massive embolus. The incomplete infarct is also very similar to the very early stage of a true infarct and it is therefore quite plausible that all these lesions begin the same way, but that the condition of the lung dictates its course—the infarct remaining incomplete in the normal lung and going on to completion when there is disturbance in the collateral circulation, as for example in congestive heart failure.

### SUMMARY AND CONCLUSIONS

- 1. Roentgenological examination of the lungs after death is a definite aid in the pathological examination.
- 2. A description is given of a routine method of taking postmortem teleroent-genograms and of preparing the lungs by a formalin injection-inflation technique in order to permit an accurate correlation between the anatomic lesions in the lung with those demonstrated on the roent-genogram.
  - 3. From a study of over 3,500 autopsies

the incidence of apparent increased frequency of pulmonary embolism and infarction is emphasized and special note is made of the higher proportion among medical rather than surgical patients.

- 4. The gross and microscopic pathology of pulmonary embolism and infarction is reviewed.
- 5. The size, shape, usual locations, and the peripheral nature of infarcts are described. Infarcts of the lung are always in contact with pleural surfaces, and the long axis of the infarct is parallel to the longest pleural surface it involves. The cardiac margin of the infarct is convex or "hump" shaped.
- 6. Special attention is called to healing and healed infarcts, lesions which produce linear shadows on the roentgenograms and which are more easily recognized by the described method of examination.
- 7. The term "incomplete infarction" is suggested for the syndrome characterized by pleural pain or blood spitting or both, associated with a rapidly appearing and disappearing infarct-like area of consolidation in the lung without alveolar wall destruction. This is shown to be similar to the oft-repeated experimentally produced lesions which had been previously ignored as regards clinical application.
- 8. Although the correlation of the clinical findings of the cases in this study has not been fully completed, it is apparent that:
- a. There is often insufficient clinical evidence of pulmonary infarction to allow a diagnosis; for example, there may be no pleural pain, blood spitting or any obvious source of an embolus, but given any one of these findings, together with roentgenological evidence consistent with an infarct, the diagnosis may be made.
- b. In view of the fact that one-third of the cases of pulmonary infarction occur in patients who have not been operated upon and who have no demonstrable cardiac disease, it is important to consider pulmonary infarction in the differential diagnosis of pulmonary disease in ambulatory patients.

c. An accurate diagnosis of pulmonary infarction is very important because unless proper treatment is carried out the patient may have a fatal embolus.

#### REFERENCES

- 1. Rössle, R. Ueber die Bedeutung und die Entstehung der Wadenvenenthrombosen. Virchow's Arch. f. path. Anat., 1937, 300, 180-180.
- MEANS, J. H., and MALLORY, T. B. Total occlusion of right branch of pulmonary artery by an organized thrombus. Ann. Int. Med., 1931, 5, 417-427.
- 3. Cutler, E. C., and Hunt, A. M. Postoperative pulmonary complications. *Arch. Int. Med.*, 1922, 29, 449-481.
- 4. BARDIN, PIERRE. L'embolie pulmonaire. Masson et Cie, Paris, 1937.
- 5. Steinberg, B., and Mundy, C. S. Experimental pulmonary embolism and infarction. *Arch. Path.*, 1936, 22, 529-542.
- COHNHEIM, J., and LITTEN, M. Ueber die Folgen der Embolie der Lungenarterien. Virchow's Arch. f. path. Anat., 1875, 65, 99–115.
- LITTEN, M. Untersuchungen über haemorrhagischen Infarkte. Ztschr. f. klin. Med., 1879, 1, 131–227.
- 8. Karsner, H. T., and Ash, J. E. Studies in infarction. II. Experimental bland infarction of the lung. J. Med. Research, 1912–13, 27, 205.

#### DISCUSSION

Dr. H. Dabney Kerr, Iowa City, Iowa. It is a pleasure to be able to discuss such a paper as has been presented by Drs. Castleman and Hampton. We always expect something good to come out of the Massachusetts General Hospital and we certainly have not been disappointed this time.

There has been very little theorizing in the presentation of this excellent work, and we have been given a maximum of factual evidence, which, it seems to me, is one of the things which we as roentgenologists need most. Certainly all of us have been puzzled by various shadows seen in the antemortem films and even in the postmortem films of inflated lungs which we may have taken, but it seems to me that the work which has just been presented is a tremendous help to us because it shows us basically the causes of these shadows over which we may have theorized but which we were unable to explain adequately.

Roentgenologists need this type of basic,

fundamental pathologic and anatomic verification of the shadows which they see on films. I can plainly see how this can be an aid to us. It gives us a much better insight into the pathologic processes with which we are concerned and which we commonly encounter. It is also an example to us, those of us who may think we are terrifically busy and thereby put aside the basic explanation of roentgenologic findings, because certainly if anyone is busy it is the group at the Massachusetts General Hospital. Yet they have taken time to give us this exceedingly important and clarifying paper.

Dr. Castleman has told me that at least 30 per cent of their cases of proved infarction and embolism have occurred in noncardiac medical patients. That, to me, was very illuminating because it is not usually thought that noncardiac medical patients and nonsurgical patients have these infarcts.

It has been interesting to me also to notice that the shape of these lesions is not always the so-called triangular shadow; that the position of the infarct, particularly in the majority of cases where they are found at the bases, is not that of the triangle with the base to the periphery but is more likely to show either an oval or a triangular shadow with the base medial and the apex peripheral. They have given us both in the pathologic specimens and on the films very adequate explanation for these fir dings.

I think this is undoubtedly one of the best papers giving us a fundamental explanation of the pathological findings in the chest that we have had the pleasure and opportunity of hearing for a long time.

DE. GEORGE W. HOLMES, Boston. I would like to add a brief statement as to the practical value of this method of examining the chest; perhaps I should not say "add," but "emphasize."

First, most of these patients are too sick to be brought to the roentgen department for examination and that means that the examination must be made at the bedside. We need better portable apparatus than we are usually equipped with to do the best work. To do our best work, we should be able to take a film at the bedside in one-twentieth of a second. Such apparatus is now available in some clinics.

The second point which I would like to make is that a single examination, as Dr. Hampton R



pointed out, may be negative and we should be given the opportunity to examine these patients more than once and on different days.

Then, I would like to emphasize again the peculiar character of these shadows. They are not what we expect to see.

I want to thank Dr. Kerr personally for emphasizing in his discussion the amount of work that these men have done.

DR. DAVID S. DANN, Kansas City, Mo. I would like to make one or two comments that occurred to me.

Of course, all of us here undoubtedly feel, as I do, the great value of this fundamental piece of work and feel the justification for the careful correlation between the pathologic and the roentgenologic departments, and undoubtedly that will explain away many embarrassing

moments that most of us have had at one time or another.

I have been very much interested in the statement concerning the emboli occurring postpartum; that is, noncardiac in nature, and it occurs to me now, as I recall seeing sections presented by our pathologist in which he demonstrated emboli of placental cells occurring normally, I wonder whether these emboli which have been demonstrated in this fashion may not represent such embolic phenomena.

Dr. Castleman (closing). In answer to Dr. Dann's question about placental cells, I must admit that I have not heard of it. However, the occurrence of incomplete infarction in post-operative patients as well as the postpartum would seem to indicate that embolic placental cells, if true, is not an adequate explanation.



# CYSTIC BRONCHIECTASIS\*

# A CLINICAL AND ROENTGENCLOGICAL STUDY

By DAVID REISNER, M.D., and I. G. TCHERTKOFF, M.D. NEW YORK CITY

YSTIC disease of the lung has attracted considerable attention in recent years as indicated by the rapidly accumulating literature on this subject. There is no doubt that cases of pulmonary cystic lesions are being observed with increasing frequency. In a large measure this is probably due to the fact that this condition is at present more readily recognized than heretofore. Another reason, however, may be the increasingly wide use of routine roentgenographic examinations of the chest. both in general hospital practice and in apparently healthy individuals. In a number of instances pulmonary abnormalities that may otherwise have remained undetected are thus brought to light.

It is not the purpose of this paper to enter into a full discussion of the various forms of air-containing cystic changes in the lung, but to call attention to a particular type of lesion, examples of which are often included in reports on cystic pulmonary disease. We refer to cases which have been variously designated as "polycystic lung" (Bagliani3), "bronchiectasis universalis cystica" (Dániel and Jezsovics<sup>8</sup>), or "open honeycombed lung" (offene Wabenlunge, Lenk19). From a purely morphological point of view it may be said that pulmonary changes of this type occupy a somewhat border line position between cystic formations and saccular bronchiectasis inasmuch as they combine certain characteristic features of both. However, our observations would tend to indicate that this lesion represents a well defined entity characterized by distinct clinical and roentgenographic features as well as by corresponding pathological changes. It therefore seems justified to separate cases of this type, on the one hand, from other forms of

cystic disease of the lung and, on the other, from common bronchiectatic lesions resulting from valious inflammatory processes. In addition, t is of particular practical importance to differentiate such lesions from pulmonary tuberculosis as will be brought out in the subsequent discussion.

This report is based on a group of 17 cases which were observed on the Tuberculosis Services of the Metropolitan and Sea View Hospitas and in the Tuberculosis Clinics of the Department of Health. While the total number of cases studied was considerably large some were eliminated from this report, sincer because of insufficient data or because of complicating features which rendered the identification of the original character of the lesion rather difficult.

# CUITICAL ASPECTS

Of the 17 cases, 12 were males and 5 females. Sixteen were white and 1 was colored. The ages ranged from eleven to seventy years. There were 3 patients, eleven, thirteen and four men years old respectively at the time of the first observation. The age factor as found in this series of cases cannot be regarded as of any particular significance. The fact that the majority of the individuals were a fulls is explained by the general nature of the material at our disposal.

History and Symptoms. In a large proportion of the cases symptoms attributable to the respiratory trait were either entirely absent or very mile. This was often quite out of proportion with the marked physical signs and, even more so, with the extent of the pulmonary changes as demonstrated on roentgen studies. In a number of instances the pulmonary condition was discovered on

<sup>\*</sup> From the Sea View Hospital, Staten Island, N. Y., the Tuberculosis Division of the Metropoita. Hospital, and the Clinics of the Bureau of Tuberculosis of the Department of Health, New York City.

routine roentgenograms. This was the case in 7 patients of this group.

Of the 17 cases, 4 had practically no complaints referable to the respiratory organs. In 8 patients the symptoms were quite mild, such as recurrent "chest colds" or "bronchitis," slight chronic cough of many years' duration, either dry or associated with expectoration of scanty sputum. The remaining 5 cases presented more definite symptoms, such as more or less severe cough, usually exceedingly chronic, with or without expectoration. In some cases the symptoms appeared to be subject to seasonal exacerbations, usually during the winter months. In none of the cases was the expectoration fetid in character. Two patients gave a history of a single hempotysis during the entire course of illness of many years' duration. In one of these there was evidence of a cardiovascular complication with signs of congestive failure. Several patients complained of progressive shortness of breath on exertion. This was observed in individuals of advanced age with pulmonary emphysema or cardiovascular complications. Constitutional signs and symptoms, such as fever or loss of weight and strength, were absent in the uncomplicated

Aside from the usual childhood diseases, the past histories did not contain any significant data, especially as regards preceding respiratory affections. Only 2 patients had a history of pneumonia in the past. While the actual date of onset of the symptoms and their total duration were extremely difficult to determine because of the mild and rather vague character of the complaints, it is noteworthy that a number of cases dated the onset of their symptoms to early childhood. In others, a history of twenty years' duration or more could be obtained.

Physical Examination. In the absence of complications the general condition shows little, if any, impairment. This is, of course, different in cases showing signs of either chronic respiratory infection, emphysema or circulatory embærrassment. Varying de-

grees of dyspnea and cyanosis were found in several of the older individuals, evidently due to coexisting emphysema or cardiovascular complications. Clubbing of fingers, was found in 3 cases, all of whom showed evidence of either chronic pulmonary infection or congestive cardiac failure.

Examination of the chest as a rule shows no visible deformity or retraction of the thoracic wall. The percussion note over the involved area is variable, that is, either impaired, or of normal resonance, or else hyperresonant, depending upon the extent of involvement and the coexisting emphysema. The breath sounds are either bronchovesicular or bronchial, but at times diminished in intensity. Almost invariably one finds numerous moist râles of medium or coarse size and many rhonchi. Since these signs are often particularly pronounced over the upper lobes, it is quite understandable that an extensive tuberculous process is frequently suspected in these cases.

Laboratory Findings. The usual laboratory examinations did not disclose any relevant findings. The sputum was consistently negative for tubercle bacilli in all but one case in which the roentgen findings indicated the presence of a complicating tuberculous lesion. The absence of tubercle bacilli from the sputum merits particular emphasis in view of the fact that the majority of the cases of this series was referred for institutional care with the diagnosis of pulmonary tuberculosis. A number of the cases had been in tuberculosis hospitals or under clinic supervision over a period of many years. The blood Wassermann test was positive in 2 cases. Although lues has been referred to by some authors (Sandoz,<sup>24</sup> Balzer and Grandhomme<sup>4</sup>) as a possible etiologic factor in this type of pulmonary lesion, it seems reasonable to regard the presence of a luetic infection as a mere coincidental finding.

# ROENTGEN FINDINGS

Roentgen examination provides most pertinent information as to the location of

the lesion, its distribution and, above all, an accurate portrayal of the morphologic character of the changes.

The extent of involvement varies greatly in the individual cases. In most cases, however, the lesion occupies rather large areas of the lung, such as the greater portion of one lobe, a whole lobe, or even several lobes. Table 1 indicates the distribution and the extent of involvement as found in this series. It will be noted that there was a marked predominance of cases in which the right lung was involved. Another noteworthy point is the frequent involvement of the upper lobe. This deserves particular mention as it may be of value in distinguishing lesions of this type from ordinary saccular bronchiectases which, as is generally known, are more commonly situated in the basal portions of the lung. On the other hand, it is well to remember that the frequent location in the upper lobes may cause difficulties in differentiating such changes from tuberculous lesions.

The characteristic roentgenographic findings are as follows: The involved portion of the lung shows a honeycomb- or sponge-like appearance and often gives the impression of a bizarre network composed of meshes of various sizes. This appearance is produced by a cluster of thin-walled, closely packed cavities separated by fine trabeculations. The cavities are usually round or ovoid, at times their borders are polygonal or irregular. This bizarre structure is evidently due to overlapping of the borders of the cavities located in various planes of the involved pulmonic area. The size of the cavitations is variable, usually ranging from that of a pea to that of a walnut. Small fluid levels are often noted at their lower poles especially in those situated in the more dependent portions of the lung. Changes indicative of a chronic inflammatory process, such as marked fibrosis or shrinkage of the lung, are as a rule absent in uncomplicated cases of cystic bronchiectasis. In most cases there is no evidence of alteration in the position or shape of the mediastinal structures or heart, no narrowing of the intercostal spaces and no distortion of the contours of the thorax. The aeration of the involved portions of the lung shows little impairment and its volume does not appear appreciably reduced although the lesion may be quite extensive.

The roeatgenographic findings just described represent the basic and character-

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	No. of
Right upper lobe	
Right midd e labe	I
Right upper and middle lobes	2
Right miccle and lower lobes	1
Right upper, middle and lower lobes	2
Left upper lebe	1
Massive involvement of total left lung	2
Bilateral involvement	2
	***************************************
Total	17

istic pattern of the lesion. Some cases, however, show mere or less pronounced deviations from the typical appearance, chiefly varying degrees of surrounding fibrosis and infiltration with resulting retraction of the pulmonic field. Such additional changes are indicative of a superimposed chronic inflammatory process. The typical picture of the lesion is generally clearly preserved in young individuals. Complicating features are more apt to be found in older persons, especially in cases presenting marked subjective symptoms and a history of recurrent respiratory infections of many years' duration.

A type of lesion which may represent a somewhat different entity was found in 2 cases included in this report (Cases XVI and XVII). While the clinical picture of these cases seemed to conform with the one observed in the other cases of this group, the roentgen findings were somewhat different, inasmuch as there was marked contraction of the pulmonic field accompanied by displacement of the mediastinal structures and heart. Massive involvement of an entire lung with complete absence of functioning parencayma may account for this

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roentgenographic picture. A case in which the roentgen findings were practically identical with those just mentioned was recently reported by Gale, Keeley and Coon<sup>13</sup> following pneumonectomy.

Bronchographic examinations were carried out in a cases of this series. In nearly all of these cases the contrast material readily entered and filled the above described cavities. This demonstrated that they represented saccular dilatations communicating freely with the bronchial tree. Some of the cases also showed cylindrical and fusiform bronchiectasis leading directly into the dilated sacs. There were, however, no indications of distortion or irregularity in the shape or course of the saccular or cylindrical dilatations, as contrasted with ordinary bronchiectasis of inflammatory origin where such findings are usually present.

#### FATHOLOGY AND PATHOGENESIS

A perusal of the literature disclosed only few reports on the pathological findings in cases which clinically and roentgenographically were comparable to those discussed in this paper. Such instances were reported by Herms and Mumme, <sup>16</sup> Weiss, <sup>28</sup> Canigiani, <sup>6</sup> Nolte, <sup>20</sup> and quite recently by Sellors. <sup>26</sup> A similar case is mentioned by Aschoff. <sup>2</sup> One of our cases (Case XIV) came to necropsy and the findings are included in the case report.

The gross findings are as follows: A large portion of the lung, usually one or more lobes, is transformed into a cluster of thinwalled, cyst-like cavities of variable sizes which communicate freely with the bronchial branches and sometimes with each other. These changes give the involved portion of the lung a characteristic sponge-like appearance. The cavities have a smooth and shiny inner surface and frequently contain small amounts of mucoid secretion. In addition to the cyst-like sacs there are also fusiform and varicose dilatations of the larger bronchial branches which show a regular even lumen and often lead directly into the saccular dilatations. The pulmonary parenchyma is either absent or considerably reduced, the remaining alveoli showing emphysematous changes. The yellowish-white color of the involved area, due tomarked diminution or absence of anthracotic pigment, contrasts with the dark discoloration of the adjacent normal portions of the lung.

Microscopic examination reveals that the walls of the cystic dilatations contain the structural components of the bronchial walls, namely, muscle, cartilage, mucous glands and epithelial lining. The amount of cartilage and muscle shows considerable variation, from complete absence in some cases to irregular proliferations in others. The epithelial lining is of a true bronchial type and consists either of several layers of cylindrical ciliated cells, or of a single layer of either cylindrical, cuboidal or flat cells (Sellors). The septa between the sacculations consist of a thin layer of loose or compact connective tissue. At times there is an excessive amount of fibrous tissue between the cavities. Some cases, however, show, in addition to the above findings, varying degrees of subacute and chronic inflammatory changes with more or less extensive bronchitis and peribronchitis. Such changes are evidently the result of superimposed infection which is bound to complicate the original condition and cause a marked alteration of the typical anatomic findings.

While the anatomic and morphologic character of the pulmonary changes just described appears quite well defined, the question as to the pathogenesis cannot be regarded as having been satisfactorily answered as yet. In considering the pathogenetic aspect of cystic bronchiectasis, it seems necessary to refer briefly to the pathogenesis of cystic disease of the lung in general.\*

One type of pulmonary cystic lesion has been considered as due to a congenital neoplasia and designated as "fetal cystic bronchial adenoma" or "cystadenoma"

<sup>\*</sup> It should be mentioned in this connection that only air-containing cystic lesions of the lung are considered in this paper.

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cystic disease of the lung and, on the other, from common bronchiectatic lesions resulting from various inflammatory processes. In addition, it is of particular practical importance to differentiate such lesions from pulmonary tuberculosis as will be brought out in the subsequent discussion.

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# CLINICAL ASPECTS

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# ROENTGEN FINDINGS

Roentgen examination provides most pertinent information as to the location of (Stoerk,<sup>27</sup> Couvelaire<sup>7</sup>). In these cases the larger bronchi were found to be normally formed, while the lung parenchyma appeared to be replaced by numerous small cysts and a stroma containing gland-like epithelial proliferations. It is obvious that there is no similarity between this form of cystic disease and the type referred to in this report as cystic bronchiectasis.

Some investigators postulated intrauterine inflammatory processes resulting in stenosis of the bronchi as a cause of cystic changes in the lung (Grawitz,14 Stoerk27). It is quite probable that bronchial stenosis plays a certain rôle in the formation of the large sac-like or "balloon" type of cysts which are often connected with the bronchial tree by a very narrow opening (Dehio,9 Pollock and Marvin,22 Anspach and Wolman, and others). This mechanism. however, could hardly account for the formation of the cystic variety of bronchiectasis since the latter show no evidence of bronchial stenosis. In fact, the presence of a wide open communication with the bronchial tree must be regarded as one of the typical features of this condition.

Other observers, especially Heller, <sup>15</sup> thought that fetal atelectasis with consecutive hyperplasia and dilatation of the bronchi might be responsible for the origin of the "sponge-lung" or cystic type of bronchiectasis. This assumption, however, fails to explain the fact that such changes have been found in the newborn.

The majority of the writers on the subject are inclined to regard as the most important cause of cystic lesions of the lung an arrested development of the bronchial tree combined with agenesia of the pulmonary parenchyma (Hueter, Hückel, Tode Lange, Chenck, Schenck, Schenck, and others).

It may not be amiss to recall here some of the essential facts concerning the embryonal development of the lungs and bronchi. It is well known that the bronchial tree develops from successive dichotomous subdivisions of the trachea and stem-bronchi. Pulmonary alveoli appear as small lateral sacculations of the terminal bronchioli

during the fifth and sixth months of intrauterine life. If the normal subdivision of the bronchial tree is impeded at a certain phase of the embryonal development, no lung parenchyma will be formed and the already existing bronchial ramifications may continue to grow into abnormally large spaces. Following the inflation of the lungs after birth these spaces will become distended and form cystic air sacs.

It is conceivable that the variations in the types of pulmonary cystic formations, especially as to size and number, depend to a great extent upon the stage of intra-uterine life at which the arrest in the development of the bronchopulmonary structure occurs. If its growth is impeded in the early period of embryonal development, at a time when only the stem-bronchus or the lobar branches have been formed, the parenchyma of an entire lung or of a lobe will be absent and the resultant malformation may be one or several large cystic sacs. This may be the mechanism for the formation of large solitary or multiple cysts, most of which are encountered in infants and in young children (Anspach and Wolman,1 Ribadeau-Dumas and Rault, 23 Eloesser, 12) on rare occasions only in adults (Dehio.9 Wood?). If, on the other hand, the development is arrested late in fetal life, that is after the evolution of the bronchial tree has progressed to the stage of subdivision into small or terminal bronchioli, but before the formation of the pulmonary alveoli, the result may be an ectasia of numerous small bronchioli, a condition sometimes described as diffuse bronchiolectatic emphysema.

The cystic form of bronchiectasis, which is the subject of the present report, may be said to occupy an intermediary position between the large cystic sacs and the bronchiolectatic cystic disease. An impeded development of the bronchial tree occurring after the large and the medium sized branches have been formed, which prevents their further subdivision into smaller ramifications, may explain the origin of this type of cystic dilatations of the bronchi.

It should be pointed out, however, that

the pathogenesis of cystic disease of the lung in general and of the cystic form of bronchiectasis in particular is not completely understood as vet, since so much of it is purely conjectural. It is quite conceivable that the resultant changes represent the combined effect of more than one of the above mentioned causes. A combination of an impeded development with a defective supporting stroma and insufficiently formed elastic elements, as emphasized by Pepere<sup>21</sup> and Bard,5 must also be considered as one of the possibilities. Furthermore, it should be mentioned that it is not always possible to draw a sharp line of division between the individual types of cystic formations and that some cases may combine characteristic features of two different groups (Dustin;11 see Case xvi of this series).

It must be admitted that direct and unequivocal proof of the congenital origin of cystic bronchiectasis is extremely difficult to obtain, even in the presence of necropsy findings, unless observed in a very young infant. This, however, is rarely the case as this condition is seldom, if ever, the direct cause of death in that age. In older individuals, on the other hand, superimposed chronic inflammatory changes may often obscure the original character of the lesion. The following pathologico-anatomic features, however, may be regarded as important criteria in favor of the congenital nature: the lack of anthracotic pigmentation in the involved portion of the lung; the regularity in shape and distribution of the saccular dilatations; their wide open communication with the bronchial tree; the frequent predilection for the cranial portions of the lung; and the absence of marked inflammatory changes, in contrast to the cases of ordinary bronchiectasis of a comparable extent.

A number of clinical indications lend support to the concept of the congenital origin, namely: the disproportion between the frequent asymptomatic or extremely mild clinical course on the one hand, and the extent of the pulmonary changes on the other; the insignificant past history, especially as regards past respiratory infections; and the fact that in many cases the onset of the symptoms may be traced back to early childhood. To this must be added the characteristic roentgen findings which are strikingly different from the changes observed in the common forms of bronchiectasis.

#### DIFFERENTIAL DIAGNOSIS

In the differential diagnosis of cystic bronchiectasis the following conditions deserve particular consideration: saccular bronchiectasis resulting from chronic inflammatory processes; tuberculosis; emphysematous bullae; and other forms of cystic disease of the lung.

- (1) Saccular Bronchiectasis. The clinical and roentgenological distinction between ordinary saccular bronchiectasis and the honeycomb- or sponge-lung characteristic of cystic bronchiectasis was repeatedly stressed in the foregoing paragraphs and needs no further elaboration at this point. It should be remembered, however, that in some cases a differentiation from ordinary saccular bronchiectasis may be extremely difficult because of superimposed chronic infection. In fact, it is entirely possible that a number of cases with the usual clinical and roentgenographic manifestations of chronic suppurative bronchiectasis represent the end-result of an infectious process engrafted on a pre-existing honeycomb
- (2) Tuberculosis. The physical signs frequently found in cases of cystic bronchiectasis, such as altered breath sounds and numerous moist râles over the upper lobes, very often suggest an erroneous diagnosis of pulmonary tuberculosis. The scant subjective symptoms, the good general condition of the patient and the non-progressive clinical course, present a striking contrast to the physical signs and are important points against tuberculosis. Roentgenologically, the differentiation from secondary bronchiectasis due to chronic fibroid phthisis is based chiefly on the absence of extensive fibrosis and contraction of the

lung which are characteristic for the cirrhotic-indurative forms of chronic pulmonary tuberculosis. The distinction between cystic bronchiectasis and tuberculous parenchymal cavities rests on the typical spongelike structure, the multilocular thin-walled appearance of the annular formations and the absence of any changes indicative of an infiltrative process in the former. The persistent absence of tubercle bacilli from the sputum is, of course, a decisive point against tuberculosis, especially in view of the roentgen findings indicative of cavitations. It should be mentioned, however, that occasionally tuberculosis may be a complicating feature of cystic bronchiecta-

(3) Emphysematous Bullae. From a roentgenographic standpoint only multiple small or medium sized bullae may have to be considered in a differential diagnosis of cystic bronchiectasis. Large or so-called "giant" emphysematous bullae resemble more closely the large "balloon" type of pulmonary cyst. In contrast to cystic bronchiectasis, emphysematous bullae rarely show well circumscribed complete ring shadows. The presence of multiple fluid levels, often found in cystic bronchiectasis, speaks against emphysematous bullae. It should be kept in mind, however, that a more or less marked degree of diffuse emphysema, with or without demonstrable bulla formation, is not infrequently associated with cystic bronchiectasis, particularly in older individuals.

(4) Other forms of cystic disease of the lung, especially large solitary or multiple cysts, are found mostly in infants and young children, whereas cystic bronchiectasis may be observed in any age. The former usually cause quite marked symptoms of respiratory distress with signs and symptoms of mediastinal pressure. The physical and roentgen findings are very similar to those observed in pneumothorax. Signs of intrathoracic pressure, such as displacement of the heart and mediastinal organs to the opposite side, are often present. It is evident that there is very little similarity be-

tween changes of this type and the character saic findings observed in cystic bronchiecters.

# COURSE, PROGNOSIS AND THERAPY

Our observations in this group of cases would seem to indicate that the clinical courses, on the whole, of a non-progressive character and that the prognosis is rather favorable, provided that no complications develop. In vounger persons the presence of evente bronchiectasis is apparently compatible with general good health and with complete or nearly complete absence of subjective symptoms. However, with advanzing age some of these individuals become chronic sufferers because of recurrent infections which may eventually set up a chromic suppurative process. An originally harmess anatomic abnormality is thus transformed into a serious and at times disabling illness.

Other possible complications of clinical significance are pulmonary emphysema and zardiac insufficiency, especially right heart alure. The latter may be the result of the zhronically impaired pulmonary circulation caused by extensive pulmonary changes such as are seen in some cases of cystiz bronchiectasis. The frequently associated emphysema is an additional functional burden on the right heart. Of the cases included in this report, 2 patients aged Efty-seven and seventy years respectively died from cardiac insufficiency. In these rases, however, the cardiovascular complication was apparently independent of the oulmonary lesion.

As to the therapy, it is evident that cases of ar complicated cystic bronchiectasis presenting no symptoms require no particular treatment. Certain preventive measures, however, may be of some advantage. These ind viduals should be aware of their condition and should be advised to take proper care apparently harmless respiratory infections. Otherwise, the treatment is purely symptomatic. Cases in which the original lesion is complicated by severe chronic infection should be treated along the same

lines as any other chronic suppurative bronchiectasis. Needless to say, cases of cystic bronchiectasis present no indication for surgical measures, such as lobectomy, unless complicated by a progressive suppurative process.

A final point to be emphasized is the fact that in the past these individuals have apparently often been regarded as suffering from pulmonary tuberculosis. Many of them have gone from one tuberculosis institution to another where they remained for varying lengths of time, frequently over a period of years. The unnecessary hardship as well as the hazard of exposure to tuberculous infection thus imposed on these individuals is quite obvious. The needless financial burden to the community may also be a point worthy of consideration in this connection.

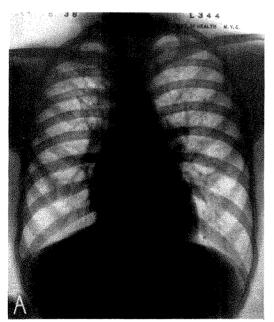
#### REPORT OF CASES

A. Uncomplicated cystic bronchiectasis. Clinical symptoms absent or very mild (Cases I to IX).

Case I. J. M., a white boy, was first seen in one of the Tuberculosis Clinics of the Department of Health at the age of fourteen. His only

complaints were frequent colds and occasional mild non-productive cough. Examination of the chest showed dullness, many coarse moist râles over the right upper lobe and few râles at the right base. There were no other significant findings. During the subsequent followup period of three years, part of which he had spent in a tuberculosis hospital, he was practically symptom-free. The sputum was always negative for tubercle bacilli. Roentgen examination disclosed a honeycomb-like structure of the right upper lobe due to multiple small thinwalled cavities without surrounding infiltration or fibrosis. There was no retraction of the lung field or distortion of the adjacent structures. On bronchographic examination the annular formations could be identified as a system of saccular dilatations of the bronchi which filled readily with the contrast material. Some of the larger bronchial branches showed fusiform widening (Fig. 1).

Case II. J. T., a white boy, aged eleven, was admitted to Sea View Hospital with a history of mild non-productive cough since the age of one. There were no other significant data in the history. Examination of the chest disclosed numerous medium and coarse moist râles over the right lung especially at the base. The sputum was negative for tubercle bacilli on numer-



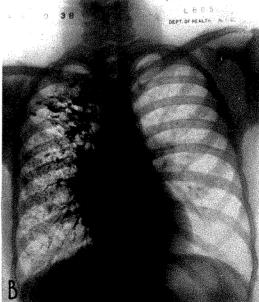
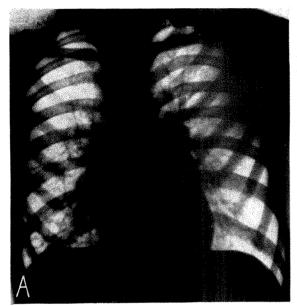
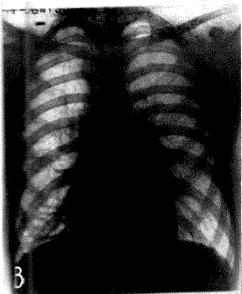


Fig. 1. Case 1. Uncomplicated cystic bronchiectasis. A shows typical honeycomb structure of the right upper lobe. Bronchogram (B) demonstrates a system of saccular bronchial dilatations and fusiform widening of the larger bronchial branches in the right upper lobe.

ous occasions. He left the hospital after sixteen months having no subjective symptoms. Roentgen examination showed a system of multiple thin-walled cavities in the lower half of the right lung with no apparent impairment of that two contained small fluid levels. Bronches aby disclosed a number of saccular and cyandical dilatations of the bronchi in the right lever lobe and few in the middle lobe (Fig. 21.





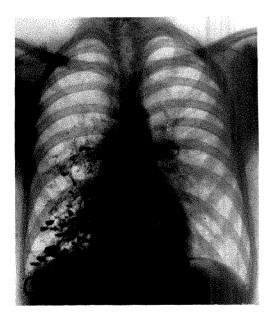


Fig. 2. Case II. Uncomplicated cystic bronchiectasis. Recatgenogram of September, 1929 (A) shows whereous thin-walled annular formations of our pying the lower two-thirds of the right lung Roentgenogram (B) taken in 1938, nine recast later, shows multiple small fluid levels which the cavities, otherwise no essential change. Seenchogram (C) demonstrates many saccalar and cylindrical dilatations of the broach in the right middle and lower lobes.

aeration or retraction of the lung field. He was seen again at the age of twenty, after a lapse of nearly eight years, when he stated that he has had no subjective symptoms and that he has been able to pursue a perfectly normal mode of life. A recent roentgenogram showed that some of the cavities had increased in size and

Case III. V. F., a white boy, aged thirteen, was a contact to a brother who had pulmonary tuberculosis and was therefore examined in one of the Tuberculosis Clinics of the Department of Heal h He gave a history of frequent colds and cough with slight mucoid expectoration since early childhood. Examination of the chest

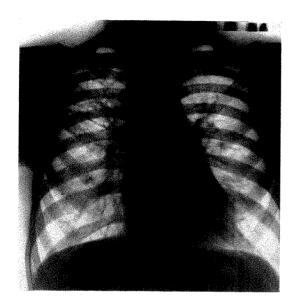


Fig. 3. Case III. Uncomplicated cystic bronchiectasis. Characteristic sponge-like structure of the right upper lobe due to a cluster of multiple thinwalled cavities.

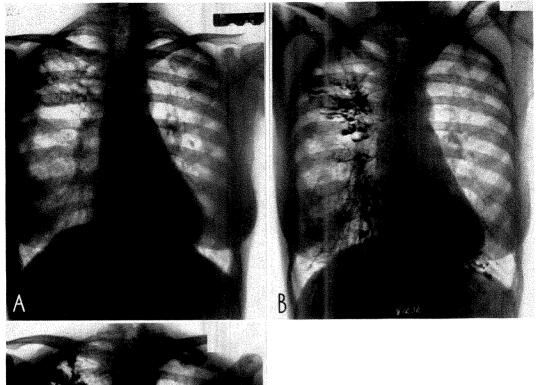
showed dullness, bronchovesicular breathing and many medium moist râles over the right upper lobe; few râles were also present at the right base. The Mantoux test was negative and the sputum showed no tubercle bacilli. Roentgen examination disclosed a characteristic spongy appearance of the right upper lobe which consisted of a network of thin annular formations without infiltration or fibrosis (Fig. 3). Bronchographic examination showed some saccular collections of contrast material in the right upper lobe and a few also at the base of the right lung.

Case IV. V. G., a white female, aged twenty-seven, was examined routinely in the course of a mass case-finding survey for pulmonary tuberculosis. She has had frequent chest colds and a chronic mild cough without expectoration. Her past history was otherwise irrelevant. Examination of the chest disclosed dullness and moist râles over the right upper lobe, otherwise no significant findings. The sputum was negative for tubercle bacilli. Roentgen examination revealed a honeycomb structure of the right upper lobe consisting of a system of thin-walled cavities some of which showed fluid levels. There was no evidence of infiltration, fibrosis or retraction of the lung field.

Case v. L. F., a white woman, aged thirty-

six, gave a history of "bronchitis" since early childhood. She was examined in the outpatient department of a general hospital where it was thought that she had pulmonary tuberculosis and she was therefore admitted to Sea View Hospital. Her past history was irrelevant. On admission she appeared to be in good general health and was entirely symptom-free. Examination of the chest revealed many moist râles and rhonchi over the entire right lung. Otherwise, there were no noteworthy findings. The laboratory data did not show anything of significance. Sputum could not be obtained for examination. She felt perfectly well and left the institution after a short stay. Roentgen examination showed numerous thin-walled annular formations throughout the right lung ranging from cherry to walnut size. In the basal portion small fluid levels were present within the cavities. The lung field appeared well aerated and there was no evidence of shrinkage of the pulmonic field or retraction of the adjacent structures.

Case vi. M. S., a white female, aged thirty, visited a maternity clinic because of pregnancy. A routine physical examination of the chest revealed signs which suggested tuberculosis and she was advised to enter the Tuberculosis Division of the Metropolitan Hospital. On admission she stated that she had had a slight non-productive cough for about one year. Her past history was irrelevant except for pneumonia in childhood. She appeared to be in good general health. Examination of the chest showed dullness, bronchovesicular breathing and numerous moist râles over the right upper lobe; a moderate number of râles were also present at both bases. There were no other significant findings. The sputum was negative for tubercle bacilli. A blood Wassermann test was positive. Roentgen examination of the chest revealed a typical spongy appearance of the right upper lobe due to numerous closely packed thin-walled cavities with marked overlapping of their borders. Small collections of fluid were seen in some of the cavities. There was no shrinkage of the lung field or retraction of the mediastinal shadow. Bronchographic studies disclosed a system of saccular bronchial dilatations in the right upper lobe. Saccular and cylindrical bronchiectasis was also present at the base of the left lung and few at the right base. She was followed for a period of six and one-half years during which time she remained



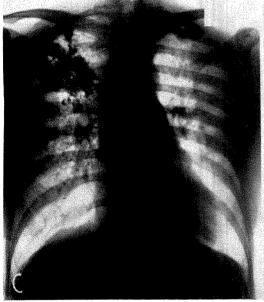
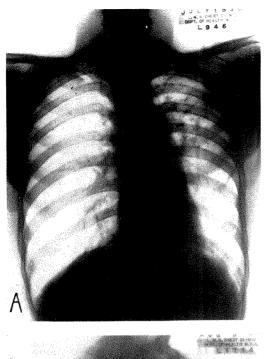


Fig. 4. Lase vi. Uncomplicated cystic bronchiectasis & shows typical spongy appearance of the right upper lobe. Note small fluid levels in some of the cavities. Bronchogram (B) demonstrates a system of saccular bronchial dilatations in the right upper lobe; saccular and cylindrical bronchiectasis is seen at the base of the left lung behind the heart and few also at the right base. Bronchogram in the prone position (C) shows the genter portion of the cavities in the right upper lobe filled with the contrast material.

practically symptom-free. There was no change in the roentgen findings throughout the entire period (Fig. 4).

Case VII. E. R., a white male, aged twentysix, was first seen in one of the Tuberculosis Clinics of the Department of Health in 1931. In 1929 he had been told that he had rulmonary tuberculosis, evidently on the basis of a physical examination. At no time did he have symptoms referable to the respiratory tract. His past history was irrelevant. Examination of the chest showed dullness, bronchovesicular breathing increased vocal fremitus and moist râles over the left upper lobe. Otherwise there were no significant findings. He was observed for a period of seven years until August, 1938, during thich time he failed to show any subjective symptoms. The objective findings remained essentially unchanged. The sputum was per stently negative for tubercle bacilli. Roentget examination showed a honeycomb



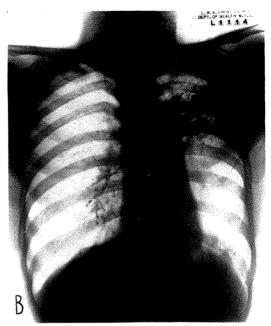




Fig. 5. Case VII. Uncomplicated cystic bronchiectasis. A, left upper lobe shows a bizarre meshwork consisting of a system of thinwalled annular formations and fine trabeculations. There is some retraction of the mediastinal shadow to the left. Bronchograms (B and C) demonstrate multiple saccular and cylindrical bronchial dilatations.

appearance of the left upper lobe from the apex to the third anterior rib with numerous thin-walled annular shadows and fine linear trabeculations. The superior mediastinum showed some retraction to the left and the intercostal spaces were somewhat narrowed in the involved area. The remaining lung fields presented an emphysematous appearance. Bronchographic studies revealed multiple saccular collections of contrast material as well

as cylindrical bronchiectasis leading directly into the saccular dilatations (Fig. 5).

Case vIII. T. M., a white male, aged thirty-three, was admitted to Metropolitan Hospital complaining of abdominal cramps and diarrhea of several weeks' duration. He had no past history or symptoms indicative of a respiratory affection. Examination of the chest revealed slight dullness, few rhonchi and fine moist

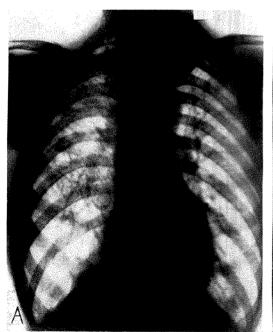
râles over the right upper lobe. There were no other significant findings. The sputum was negative for tubercle bacilli. A blood Wassermann test was positive. Roentgen examination of the chest showed a number of thin-wailed cavities occupying the right upper lobe, some containing small collections of fluid. There was no evidence of fibrosis or shrinkage, the mediastinal shadow was in normal position. Bronchographic study revealed multiple saccular and cylindrical bronchial dilatations in the right upper lobe and few saccular dilatations at the base of the right lung.

CASE IX (courtesy of Dr. D. Ulmar). J. H., a white male, aged twenty-four, had a past history of frequent colds. He complained of pain in the right lower chest and slight non-productive cough of several weeks' duration. On physical examination bronchovesicular breathing and medium moist râles were found over the right base anteriorly. There were no other abnormal findings. Roentgenograms of the chest showed multiple thin-walled caviries occupying the right middle lobe some of which contained small collections of fluid. There was

no retract in of the involved lobe or of the adjacent subsequent following the subsequent following period of eighteen months he had no subjective symptoms except a slight cough. The physical signs and the roentgen findings remained unchanged. The sputum was persistently regative for tubercle bacilli.

B. Cysic sonchiectasis complicated by chronic infessior Clinical symptoms moderate to severe. Eventgenological signs of associated chrosic suffammatory changes (Cases X to XII)

CASE X J. C., a white male, aged forty-seven, was observed at the Metropolitan Hospital for a period of nine years. He gave a history of cough associated with slight expectoration at least twenty years' duration. These symptoms were subject to seasonal exacerbations during the winter months. During the last few years the symptoms became more manad, the cough was more persistent, he expect mated moderate amounts of purulent sputure and developed progressive dyspnea on exertion. There was, however, no history of



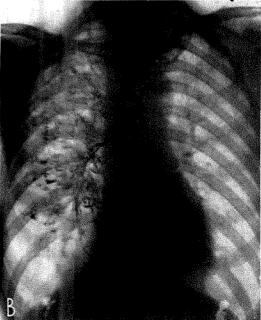


Fig. 6. Case x. Cystic bronchiectasis complicated by chronic infection. A shows multiple thin-walled cavities occupying the upper two-thirds of the right lung. Note broken and signs of shrinkage in the superior portion of the upper lobe. Diffuse emphysema of the remainder of the lung fields. Bronchogram (B) demonstrates a system of saccular bronchial dilatations in the right upper and middle lobes and fusiform widening of the descending branches.

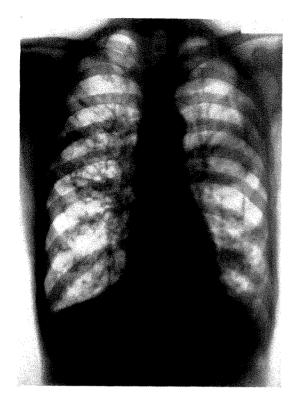


Fig. 7. Case XI. Cystic bronchiectasis complicated by chronic infection. Sponge-like structure of nearly the entire right lung and of the left basal portion. Changes indicative of a chronic inflammatory process are present at the bases, especially on the left side.

copious or bloody expectoration. It may be of interest to mention that he had spent the greater part of the twenty years in various tuberculosis institutions. On physical examination there was some retraction of the right hemithorax, dullness, bronchovesicular to bronchial breathing over the right upper lobe, many medium and coarse moist râles over the greater portion of the right lung and signs of emphysema at both bases. There was slight clubbing of the fingers. The physical findings remained essentially the same during the entire period of observation. His general condition appeared to be fairly stationary. The sputum never contained tubercle bacilli. Other laboratory findings were of no significance. Roentgen examination showed that the upper and middle lobes of the right lung were occupied by multilocular thin-walled cavities of pea to walnut size. Small fluid levels were seen in some of the cavities. In the upper portion of the right upper lobe there was a moderate degree of fibrosis

with narrowing of the intercostal spaces and retraction of the trachea to the right. The remaining lung fields showed diffuse emphysema. These findings remained essentially the same throughout the follow-up period. Bronchography demonstrated that the described cavities represented saccular bronchial dilatations communicating freely with the major bronchial branches. There was also cylindrical and fusiform dilatation of the bronchi in the right upper and middle lobes (Fig. 6).

Case xI. E. G., a white male, aged fortyeight, presented a history very similar to the preceding case, that is, a mild chronic cough with scanty expectoration and seasonal exacerbations for about twenty years. These symptoms increased in severity during the more recent years simultaneous with development of progressive dyspnea. For many years he had. been a patient in various tuberculosis hospitals and was observed at Metropolitan Hospital for a period of nine years. Examination revealed moderate dyspnea and cyanosis and slight clubbing of the fingers. There were signs of diffuse emphysema and numerous medium and coarse râles throughout both lungs as well as many rhonchi at the bases. The laboratory data showed no significant findings. The sputum was always negative for tubercle bacilli. Roentgen examination showed that the greater portion of the right lung was occupied by a bizasre network composed of numerous closely packed thin-walled cavities producing a characteristic sponge-like appearance. The left lung showed emphysema in the upper twothirds and a honevcomb structure in the basal portion, similar to the corresponding area on the right side, with changes suggestive of a chronic inflammatory process. The linear densities in the left upper portion suggested calcified pleural plaques. Bronchographic examination was not performed (Fig. 7).

CASE XII. P. O., a white male, aged fifty-four, has been under observation at the Metropolitan and Sea View Hospitals for a period of eleven years. His history and symptoms closely resembled those of the preceding two cases. He had a chronic cough and scanty expectoration of many years' duration with seasonal exacerbations, increasing severity of symptoms in recent years and progressive dyspnea. He, too, had been a patient in various tuberculosis institutions for many years. Examination of the chest

revealed dullness over the right upper lobe, bronchovesicular breathing, many moist râles and rhonchi over the right upper and middle lobes. The sputum was persistently negative for tubercle bacilli. There were no other laboratory findings of significance. Roentgen examination showed numerous cavities of various sizes in the right upper and middle lobes, the largest being about the size of a walnut. The mid-zone presented a characteristic honeycomb structure while the upper portion of the lung showed definite fibrosis and infiltration suggestive of an associated chronic inflammatory process. The remainder of the right lung as well as the left lung presented an emphysematous appearance.

C. Cystic bronchiectasis complicated by pulmonary tuberculosis (Case XIII).

CASE XIII. J. P., a white female, aged thirtyfour, applied for admission to the obstetric ward of Metropolitan Hospital because of pregnancy. She had no history or symptoms referable to the respiratory tract except eccasional chest colds. She was transferred to the Tuberculosis Division because a routine examination disclosed abnormal physical signs in the chest which suggested pulmonary tuberculosis. Her general condition was good, constitutional signs and symptoms were absent. Examination of the chest showed numerous medium and coarse moist râles throughout both lungs from apex to base. There were no other significant findings on physical examination. The sputum, which at first contained tubercle bacilli on several occasions, became persistently negative two months after admission. Bronchoscopy did not disclose any abnormal findings. Roentgen examination revealed a sponge-like structure of both lung fields due to numerous thin-walled cavities with occasional fluid levels. In spite of the extensive changes the pulmonic fields appeared to be well aerated, except in the left apex which showed a diffuse density with an area suggestive of a small cavity. The latter findings were interpreted as due to a complicating tuberculous lesion. Bronchography disclosed numerous saccular and cylindrical dilatations of the bronchi in the left lung. A subsequent attempt to visualize the bronchial tree on the right side was unsuccessful. The patient was observed in the institution for a period of six months. She remained entirely symptom-free and was discharged in good general condition.

D. Cysic Conchiectasis complicated by cardiovascidar Lisease, apparently not related to the pulmonary tesion (Cases XIV and XV).

CASE XFZ. G. A., a white male, aged fiftyseven, was admitted to Sea View Hospital complaining of progressive dyspnea on exertion and distres in grouph with scanty expectoration of several months' duration. He stated that seventeen years before he had consulted a physician because of cough and expectoration and that bronchiest sis was diagnosed at that time. He was ther parently well until a few months before acmission to the hospital. Physical examination revealed bronchovesicular breathing and many coarse moist râles over the right upper lot and rhonchi at both bases. The heart was enlarged to the left. The blood pressure was 550/80. Roentgen examination of the chest showed a honevcomb structure of the right upos lobe due to a number of thin-walled cavities some of which contained small fluid levels. The increased hilar shadows and the prominent peripheral markings suggested vascular stass. On the roentgenogram the latter findings secured to some extent the other changes at the right upper lobe (Fig. 8A). During to subsequent course the patient developed emptoms and signs of progressive circulators congestion and eventually died as a result of cardiac insufficiency. The sputum was a ways negative for tubercle bacilli. Other laboratory data were essentially irrelevant.

The extopsy findings were as follows: Marked sypertrophy and dilatation of the heart especially of the left ventricle: fibrosis of the myocardium; mitral insufficiency; marked atteriosclerosis of the aorta and sclerosis of the coronary arteries; congestion of all organs. But lungs were markedly anthracotic, with the exception of the right upper lobe. The light vellowish-white color of the latter presented a striking contrast to the dark discoloration of the remainder of the lungs. On section the right apper lobe showed a sponge-like appearance and consisted of numerous thin-walled cyst-ike cavities ranging between a few millimeters and 2 cm. in diameter. There were also man- eyendrical and fusiform bronchial dilatations some of which terminated in the cystic dilatat cas. There was slight increase in fibrous tissua between the bronchial dilatations. Whatever lung parenchyma was present in this lobe appeared to be markedly emphysematous. The pleu a over the right upper lobe was thickened.

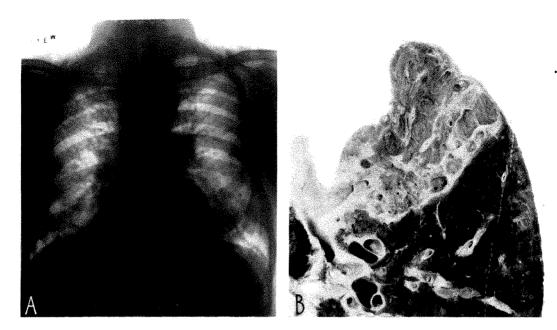


Fig. 8. Case xiv. Cystic bronchiectasis complicated by cardiovascular disease. Roentgenogram (A) shows a honeycomb structure of the right upper lobe due to multiple thin-walled cavities. The vascular markings are prominent throughout as a result of circulatory congestion. Postmortem specimen of the lung (B) showing the right upper lobe and the adjoining portion of the lower lobe. The upper lobe shows a spongy appearance and consists of numerous cyst-like saccular and fusiform bronchial dilatations. Note the light color of the upper lobe as it contrasts with the dark anthracotic pigmentation of the adjacent portion of the lower lobe.

The other pulmonary lobes showed marked anthracosis, vascular congestion and terminal bronchopneumonia (Fig. 8B). Microscopic examination showed that the walls of the cyst-like cavities consisted of muscle, cartilage, mucous glands and a small amount of fibrous tissue. Their inner surface was lined by cuboidal epithelium. In places the mucous membrane was replaced by vascular granulation tissue. The septa between the cavities consisted of fibrous tissue with some fibroblasts and lymphocytes. There was only a very slight amount of coal pigment in the apex of the right upper lobe, otherwise this lobe was free of anthracotic deposits.

Case xv. L. K., a white male, aged seventy, was admitted to Sea View Hospital with a history of chronic cough and expectoration of scant mucopurulent sputum since early childhood. During the last two years these symptoms had increased in severity. He developed progressive dyspnea on exertion and pain in the chest radiating to the shoulder. One week before admission he had a slight hemoptysis. On examination he appeared to be markedly dyspneic and orthopneic and showed pro-

nounced cyanosis. There was clubbing of the fingers. The chest was of an emphysematous type. There was no impairment of resonance on percussion. There were numerous coarse moist râles over the right lung and many rhonchi over both lungs. The heart appeared to be enlarged to the left. The peripheral vessels were sclerotic. The blood pressure was 200/90. The liver was enlarged and tender on palpation. During the subsequent course he showed signs and symptoms of progressive circulatory failure. He died eight months after admission to the hospital as a result of cardiac insufficiency. The sputum was always negative for tubercle bacilli. There were no other significant laboratory findings. Roentgen examination of the chest showed a characteristic sponge-like structure of almost the entire right lung field, due to numerous thin-walled cavities ranging between cherry and walnut size, some of which contained small fluid levels. There was no evidence of shrinkage of the lung; the mediastinum, the heart and the diaphragm were in normal position. The left lung showed marked emphysema. The heart was generally enlarged, especially to the left. Permission for autopsy was not obtained.

E. Cases with massive involvement of one jung (Cases XVI and XVII).

CASE XVI. L. C., a white female, aged thirtysix, was admitted to the Tuberculosis Division of Metropolitan Hospital in July, 1933. Her chief symptoms were chronic cough with slight expectoration since the age of five. She had had a hemoptysis on one occasion some years before admission. Her past history was otherwise irrelevant. She had been a patient in several tuberculosis institutions for several years. For a period of five years before admission to the hospital she felt well and had no sympsoms except a moderate cough. She became pregnant and applied for admission to the hospital because she had previously been told that she had pulmonary tuberculosis. On admission she appeared to be in good general condition. Examination of the chest disclosed diminished respiratory expansion of the left side with marked dullness and many coarse moist râles over the entire left lung. The heart appeared to be displaced to the left. Otherwise there were no noteworthy findings. The sputum was negative for tubercle bacilli on many occasions. The other laboratory examinations showed nothing of significance. Roentgen examination showed a sponge-like appearance of the entire left lung field due to multilocular rarefactions

of va ious sizes, the largest being located in the apical portion. There was no normal lung structure seen anywhere on the left side. The heart and the mediastinal shadow were entirely within the left hemithorax and the intercostal spaces were moderately narrowed on this side. The might lung showed marked emphysema. Bronchegraphic examination showed numerous saccular as well as cylindrical and varicose bronca eccases on the left side. It may be of interest to point out that the contrast material did not enter the large cavity situated in the apex, possibly because of a block in the bronchial wmen. The patient was discharged from the hasa al in June, 1934, in good general condition. She was seen again four years later when she stated that she had been symptomfree during this period except for a slight cough. The reentgen findings were essentially the same as above except that within the large apical cavity there could be noted a dense sharply circumscribed opacity of ovoid shape. While no definite explanation can be offered for the latter finding it is suggested that it may possibly be due to a blood clot within the cavity (Fig. 9).

CASE XII. J. L., a colored male, aged fifty, was admitted to Rikers Island Hospital complaining of frequent "chest colds" and cough with re-y little expectoration of three years'

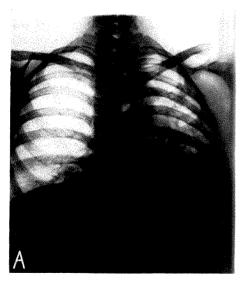






Fig. 9. Case xvi. Cystic bronchiectasis with massive involvement of the left lung. Roentgenogram of July, 1933 (A) shows sponge-like structure of the entire lung field due to multilocular rarefactions. Note large cystic formation occupying the apical and subapical area. Masked retraction of the mediastinum and heart to the left. Bronchogram (B) demonstrates multiple same when and some fusiform bronchial dilatations in the lower two-thirds. C (July, 1938) shows the appearance of the left lung five years after the original roentgenogram (Potter-Bucky technique). Note density of evoic shape within the large upper cyst.

duration. About ten years before admission he had had pneumonia on the right side, otherwise his past history was irrelevant. Examination showed flattening of the left side of the thorax and duliness on percussion. Over the left lung the breath sounds were bronchial to amphoric and there were numerous sibilant and sonorous râles. The heart appeared to be displaced to the left, the right border being at the left margin of the sternum. There was a systolic murmur over the apex and the second pulmonic sound was accentuated. The rest of the physical examination was essentially negative. He remained under observation for a period of six weeks and at the time of discharge was entirely symptom-free. The sputum was negative for tubercle bacilli. There were no other laboratory findings of significance. Roentgen examination disclosed changes of the left lung which were almost a replica of the previous case, that is, a spongy structure with a network consisting of coarse meshes, suggesting a system of closely packed cavities. Small fluid levels were seen in some of the cavities. As in the other case, no normal parenchyma could be seen on this side. There was marked retraction of the mediastinum and heart to the left with narrowing of the intercostal spaces and elevation of the left side of the diaphragm. The right lung was markedly emphysematous. Bronchographic examination was refused by the patient.

# SUMMARY AND CONCLUSIONS

- (1) A clinical and roentgenological study of a group of seventeen cases of cystic bronchiectasis is presented.
- (2) The findings observed in these cases indicate that this lesion represents a distinct entity which should be separated both from the common forms of saccular bronchiectasis and from other types of cystic disease of the lung.
- (3) The clinical symptomatology and findings are described. The frequent disproportion between the paucity of subjective symptoms and the extensive pulmonary changes is stressed. At the same time it is also brought out that in a certain proportion of the cases secondary infection may result in a chronic suppurative process.

- (4) The roentgen findings of the honey-comb- or sponge-lung characteristic of cystic bronchiectasis are described.
- (5) The pathology and pathogenesis are discussed with particular reference to the question of the congenital origin of the lesion.
- (6) The clinical and roentgenological differentiation of cystic bronchiectasis from saccular bronchiectasis of inflammatory origin, tuberculosis, emphysematous bullae and other forms of cystic disease of the lung is discussed.

#### REFERENCES

- 1. Anspach, W. E., and Wolman, I. J. Large pulmonary air cysts of infancy. Surg., Gynec. & Obst., 1933, 56, 635-645.
- 2. Aschoff, L. Pathologische Anatomie. Fourth edition. G. Fischer, Jena, 1919, 2, 312.
- 3. BAGLIANI, M. Il polmone policistico. *Radiol. med.*, 1935, 22, 1055-1077.
- 4. BALZER, F., and GRANDHOMME, A. Contribution à l'étude de la broncho-pneumonie syphilitique du foetus et du nouveau-né. Rev. mens. de mal. de l'enf., 1886, 4, 485-506.
- BARD, L. Pathogenie, evolution et traitement de la forme idiopathique des dilatations bronchiques. 7. de méd. de Lyon, 1924, 5, 381-389.
- CANIGIANI, T. Zur Kasuistik angeborener und erworbener Bronchiektasien. Röntgenpraxis, 1931, 3, 1116–1120.
- 7. Couvelaire, A. Degenerescence cystique congenitale du poumon. Ann. de gynéc., 1903, 60,
- 8. Dániel, G., and Jezsovics, K. Bronchiektasia universalis cystica. *Beitr. z. Klin. d. Tuberk.*, 1932, 80, 666-674.
- 9. Dehto, K. Ueber Pseudopneumothorax. Deutsche med. Wchnschr., 1925, 51, 817-819.
- 10. DE LANGE, C. Angeborene Zystenlunge und agenetische Bronchiektasie. *Acta paediat.*, 1927, 6, 352–372.
- 11. Dustin, A. Maladie polykystique des poumons. *Arch. de biol.*, 1931, 42, 229–249.
- 12. Eloesser, L. Congenital cystic disease of the lung. Surg., Gynec. & Obst., 1931, 52, 747-758.
- 13. Gale, J. W., Keeley, J. L., and Coon, H. M. Total pneumonectomy for congenital cystic disease of the lung. J. Thoracic Surg., 1937, 6, 626–633.
- 14. Grawitz, P. Ueber angeborene Bronchiectasie. Virchow's Arch. f. path. Anat., 1880, 82, 217- 237.
- 15. HELLER, A. Die Schicksale atelektatischer Lungenabschnitte. Deutsches Arch. f. klin. Med., 1884–1885, 36, 189–196.

16. Herms, J., and Mumme, C. Ueber kongenitale Bronchiektasie und Cystenlunge. Baitr. 2. Klin. d. Tuberk., 1931, 77, 701-716.

17. HÜCKEL, R. Beiträge zur angeborenen Wabenlunge. Frankfurt. Ztschr. f. Path., 1927, 35,

320-342.

18. Hueter, C. Ueber angeborene Bronckiestasien und angeborene Wabenlunge. Beite. = path. Anat. u. z. allg. Path., 1914, 59, 520-53

19. Lenk, R. Das charakteristische Röntgen sild der offenen Wabenlunge. Fortschr. a. d. Geb. d.

Röntgenstrahlen, 1933, 48, 418-426.

- 20. Nolte, F. A. Die Waben- und Sacklunge beim Erwachsenen und ihre Behandlung. Ergebn. d. inn. Med. u. Kinderh., 1937, 52, 256-276. (Extensive bibliography.)
- 21. Pepere, A. Della degeneratione estea del polmone. Sperimentale, 1906, 60, 171-196.
- 22. Pollock, W. C., and Marvin, H. P. Congenital cystic disease of the lung. Am. Rev. Tuberc., 1933, 27, 59-66.

- 23. READEAL-DUMAS, L., and RAULT. Dilatation ces bronches dans le jeune âge. Paris méd., 1632, 2, 381–387.
- 24. Sandon I. Ueber zwei Fälle von Bronchiektasie.

  Beite z path. Anat. u. z. allg. Path., 1907, 41,
  295-31.
- 25. Schenek S. G. Congenital cystic disease of the h.ng. Am. J. Roentgenol. & Rad. Therapy, 33, 35, 604-629.
- 26. Salloss, T. H. Congenital cystic disease of the ung Tubercle, 1938, 20, 49-71; 114-136. (Exensive bibliography.)
- 27. Sports, D. Ueber angeborene blasige Missbildunger der Lunge. Wien. klin. Wchnschr., 184. 20, 25-31.
- 28. Welse, F. H. Zur Symptomatologie der Wabenlance. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1928, 4, 230-237.
- 29. Noom B. G. Congenital cystic disease of the large. J. Am. M. Ass., 1934, 103, 815-821.



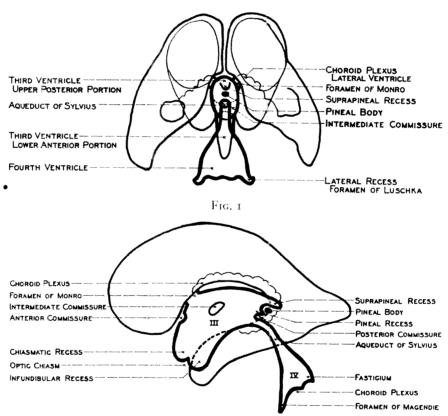
# VENTRICULOGRAPHIC LOCALIZATION OF INTRACRANIAL TUMORS\*

# III. TUMORS OF THE CEREBELLUM AND FOURTH VENTRICLE

By VINCENT C. JOHNSON, M.D., and CARL F. LIST, M.D.
ANN ARBOR, MICHIGAN

VENTRICULOGRAPHIC signs characteristic of tumors arising in the aqueduct, pons and cerebellopontine angle have been discussed in a previous communication. The purpose of this paper is to describe the ventriculographic signs produced

pathognomonic of posterior fossa tumors concern the aqueduct and fourth ventricle. Compression of these structures results in varying degrees of internal hydrocephalus always associated with tumors in this location.



F1G. 2

by tumors involving the cerebellum and fourth ventricle. Since the surgical and roentgenographic technique of ventriculography has already been described in the first paper<sup>2</sup> of this series, it is unnecessary to again discuss our methods.

It has been previously stated that changes in ventriculographic appearance

The position and shape of the aqueduct and fourth ventricle, when moderate dilatation of the ventricular system exists, have already been described. Figures 1 and 2 are again reproduced to demonstrate these relationships.

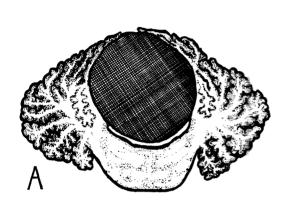
Tumors involving the posterior fossa are either extra- or intraventricular in type.

<sup>\*</sup> From the Department of Roentgenology and the Department of Surgery, Service of Dr. Max M. Peet, University of Michigan, Ann Arbor, Michigan.

The extraventricular group includes midline vermis tumors and lateralized hemispheral tumors. Although subtenterial meningiomas of the transverse sinus arise outside of the cerebellum, they will be included in the discussion of lateralized

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placement of the inferior outline of the third ventricle due to shift of the brain stem and occasionally by pressure or invasion directed upward through the incisura of the tentorium. Thus, in Figure 4, it will be noted that the inferior margin of the



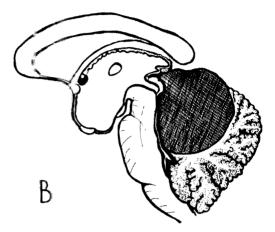


Fig. 3. A and R.

intracerebellar tumors, since the ventriculographic deformities which they may produce are similar. The intraventricular group consists entirely of those tumors which are situated completely within the fourth ventricle.

# I. Extraventricular Tumors.

a. Midline Cerebellar Tumors. Deformity and displacement of the aqueduct and fourth ventricle produced by these lesions are demonstrated by schematic drawings of the verticofrontal section (Fig. 3A), and the mid sagittal section (Fig. 3B) of a cerebellum containing a tumor of the upper vermis. The tumor represented by the densely cross-hatched area is seen encroaching upon the aqueduct and fourth ventricle from its dorsal midline position.

If the tumor occupies the dorsal vermis and extends high into the incisura tentorii, the aqueduct may be compressed at its beginning, thus simulating the ventricular deformity produced by a true neoplasm of the aqueduct (Fig. 4, Case 1). Tumors of the dorsal vermis, usually astrocytomas, may cause a slight anterior and superior dis-

third ventricle is displaced slightly upward, since this margin is not superimposed by the remporal horn, as should be the case with this degree of internal hydrocephalus.

If the tumor is situated in the lower vermis (near the foramen magnum) (Fig. 5,

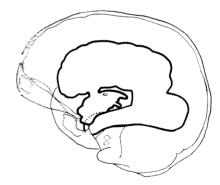


Fig. 4. Case 1 (352200).

Case 1 % not only the aqueduct but also a part of the fourth ventricle may be visualized. At operation, Case 11 was found to have a hemangioblastoma, with a large cyst in the tonsillar region. The triangular roof portion of the fourth ventricle is usually flattened by the tumor mass in this region, and only a thin streak of oxygen may

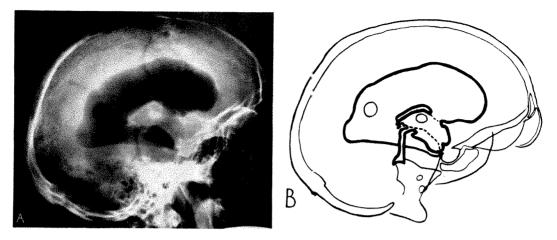


Fig. 5.\* A and B. Case # (321054).

be seen outlining the floor of the fourth ventricle. Such tumors clearly show the an-

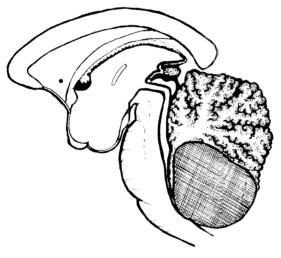
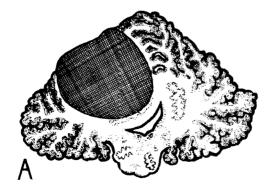


Fig. 6

teric r displacement of the pons in the lateral v ews. The aqueduct forms an angle of 70–120 degrees with the anterior outline (flocr) of the fourth ventricle, instead of the normal angle of more than 130 degrees. This type of deformity is further demonstrated by a schematic drawing of a mid sagittal section illustrating a low vermis tumor (Fig. 6).

The sagittal ventriculogram, with the occiput superior, is essential to demonstrate the midline position of these tumors; hence, in this projection the aqueduct or fourth ventricle is always visualized in the midline. Displacement of these structures to either side is characteristic of lateralized cerebellar lesions.

\* The outlines of the third ventricle, aqueduct and fourth ventricle have been accentuated by retouching in all reproduced roentge aggrams.



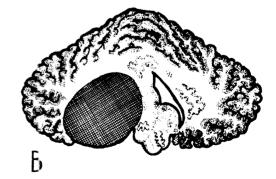


Fig. 7. A and  $B_*$ 

b. Lateralized Cerebellar Tumors. These tumors always lie lateral to the aqueduct and fourth ventricle; hence, in the sagittal ventriculogram one may expect to find

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sions in the first instance, and dorsal vermis lesions in the latter. Drawings of vertico-frontal corepellar sections illustrate the deformities caused by dorsolateral tumors

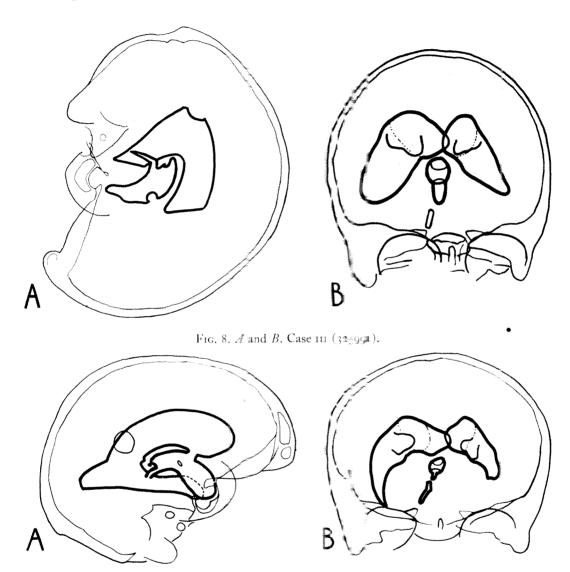


Fig. 9.  $\mathcal{A}$  and B. Case iv (2555 2).

some lateral displacement of the aqueduct and fourth ventricle away from the tumor. Since these lesions may be located either in the ventral or dorsal portion of the cerebellar hemisphere, the displacement of the aqueduct and fourth ventricle, as seen in the lateral view, may simulate the deformity produced by cerebellopontine angle le-

(Fig. 72) and ventrolateral tumors (Fig. 7B).

The lesion in Case III was found to be a cystic astrocytoma in the dorsolateral portion of the left cerebellar hemisphere. The lateral mentriculogram, with the occiput superior (Fig. 8A), shows the angulation between the aqueduct and the compressed

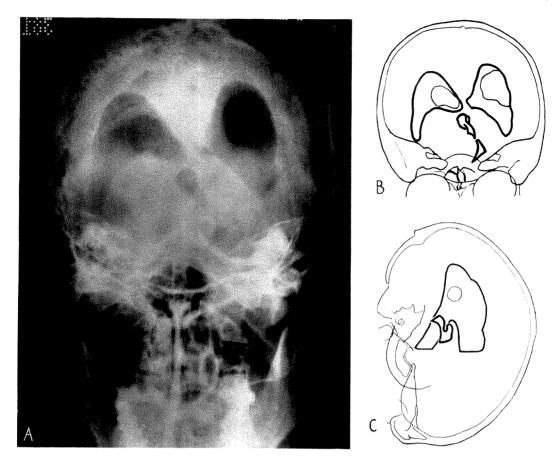


Fig. 10.  $\mathcal{A}$ ,  $\mathcal{B}$  and  $\mathcal{C}$ . Case v (381971).

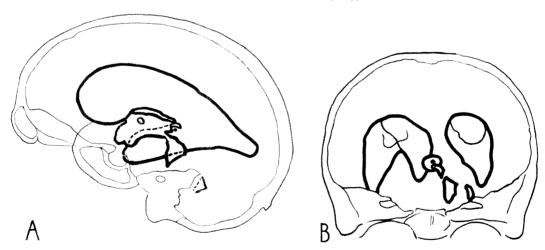


Fig. (1), A and B. Case v. (373566),

fourth ventricle, simulating the deformity produced by vermis tumors. The occipital sagittal view, on the other hand, provides positive evidence of lateralization by show-

ing contralateral displacement of the partially collapsed fourth ventricle (Fig. 8B).

The lateral displacement of the ventricular system caused by cerebellar gliomas is

similar to that produced by subtenterial meningiomas arising from the transverse sinus, since these extracerebellar lesions encroach on the homolateral cerebellar hemisphere. Cases IV and V were meningiomas

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ventricle to the side opposite the tumor. In the lateral views (Figs. 9A and 10C), the fourth ventricle is not visualized, but the aqueduct is seen to be slightly elevated in each instance and the inferior margin of the

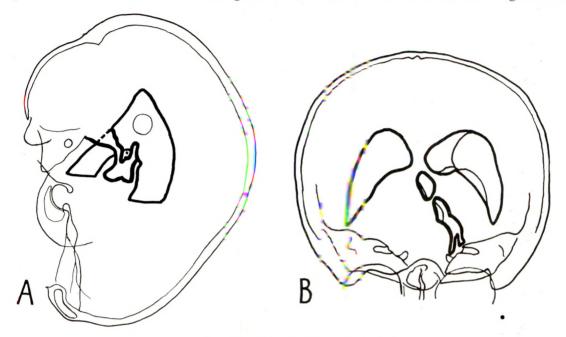


Fig. 12. A and B. Case v = (380363).

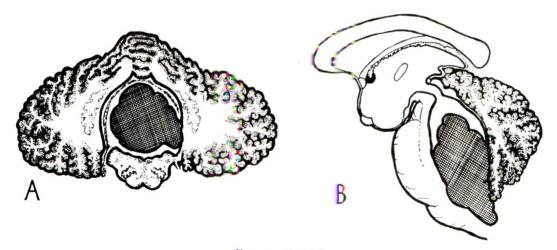


Fig. 13. A and E

arising from the left transverse sinus in the first instance, and from the right transverse sinus in the second case. Occipital sagittal ventriculograms (Figs. 9B, 10A and B) demonstrate in both cases displacement of the aqueduct and the compressed fourth

third ventricle is displaced slightly upward in Case IV. These last mentioned deformities are probably due to displacement of the brain stem by tumor pressure.

Ver rolateral cerebellar tumors also cause 2 considerable ventricular shift to the

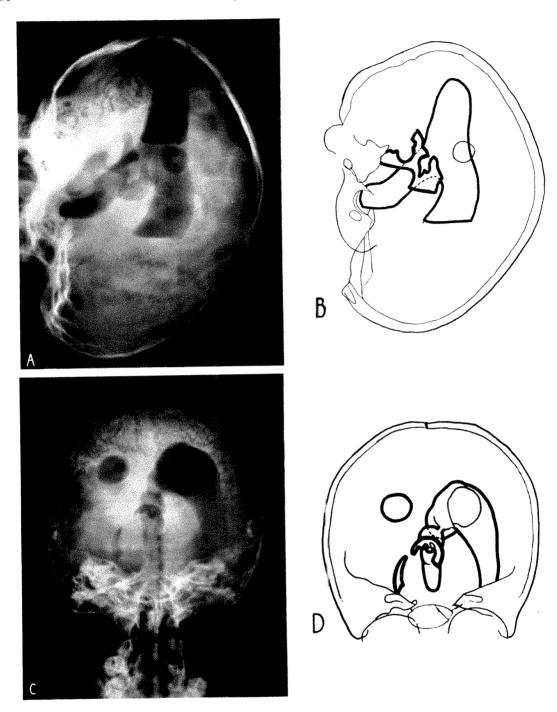


Fig. 14. A, B, C and D. Case #III (343829).

opposite side, or at least a marked filling defect on the tumor side. Tumors in this location may produce some elevation of the aqueduct and fourth ventricle; however, this was not a prominent sign associated with either of the following cases of ventrolateral tumors. A medulloblastoma in Case vi and an astrocytoma in Case vii each occupied the caudal portion of the right cerebellar hemisphere. In the lateral views of each case (Figs. 11A and 12A), fairly extensive filling of the fourth ventricle has been accomplished. The sagittal views • (Figs. 11B and 12B) demonstrate a lateral shift of the fourth ventricle and the aqueduct, a finding typical of hemispheral tumors. A localized indentation in the caudal portion of the fourth ventricle on the tumor

an intraventricular tumor sectioned in a verticofrontal plane, while Figure 13B demonstrates the same tumor in the mid sagital section. If the upper part of the tumor lies free in the cavity of the fourth ventricle, the oxygen may be traced downward along the sides of the tumor into both lateral recesses. However, this distribution of

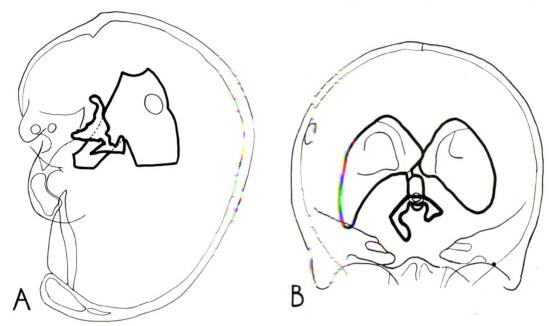


Fig. 15. A and B. Case IX (551554).

side indicates the inferior position of the tumor.

# II. Tumors within the Fourth Ventricle.

These intraventricular neoplasms obstruct the outlet of the fourth ventricle at the foramen of Magendie, thus resulting in dilatation of the entire ventricular system, including the aqueduct and fourth ventricle. The enlargement of the fourth ventricle may be also due to direct distention by the tumor. The occipital sagittal ventriculogram characteristically demonstrates the upper pole of the tumor capped by the dilated dome-shaped proximal portion of the fourth ventricle. Figures 13A and B aid in explaining the ventriculographic deformity produced by these intraventricular tumors. Figure 13A is a schematic drawing of

oxygen along the lateral margins is frequently unequal, and such inequality cannot be interpreted as diagnostic of a lateralized attachment of the tumor.

Cases VIII and IX illustrate the characteristic appearance of these lesions in lateral and occipital sagittal ventriculograms. At operation the tumor was proved to be an intraventricular ependymoma in Case VIII, and a medulloblastoma in Case IX. In the occipital sagittal views of Case VIII (Figs. 14C and D), the right lateral margin of the tumor is outlined by oxygen, while the left lateral margin is not shown, in spite of the fact that there was no attachment on this side. This inequality is also noted in the sagittal view of Case IX (Fig. 15B).

The asymmetry of the fourth ventricle produced by the intraventricular astrocy-



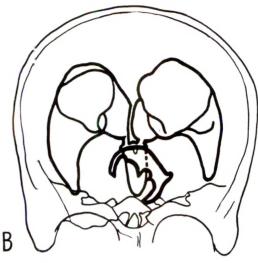


Fig. 16, A and B. Case x (379055).

toma in Case x (Figs. 16A and B) suggests wide attachment to the right ventricular wall, or perhaps invasion of the cerebellar

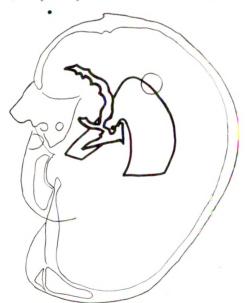


Fig. 17. Case XI (323543).

hemisphere. In this case the sign proved reliable at operation. If oxygen is fairly symmetrically distributed on either side of the tumor, one is justified in assuming midline attachment.

Fourth ventricle tumors are also very well demonstrated in lateral views, particularly in lateral projection with the occiput super or. The upper pole of the tumor divides the dilated fourth ventricle into a dorsa and a ventral recess (Figs. 14A and B, Case VIII and Fig. 15A, Case IX). The upper recess outlines the elevated roof of the fourth ventricle and the dorsal surface of the tumor, which may be nodular. A nodular outline of the dorsal surface of a cholesteatoma within the fourth ventricle is well demonstrated in the lateral view of Figure 17A, Case XI. The anterior recess is produced by the floor of the fourth ventri cle and the free ventral surface of the tumor. The angulation between the inferior border of the aqueduct and the anterior border of the fourth ventricle, typical of cerebellar tumors, may again be seen here, and is considered indicative of compression with anterior displacement of the pons. It is obvious that only the anterior recess will be inflated if the tumor has a dorsal attachment. Under these circumstances, the roentgen appearance will be similar to that found in a vermis lesion. If, on the other hand, the tumor arises from the floor of the fourth ventricle, only the posterior recess

will be visualized, and then the deformity may simulate that produced by a midline pontine tumor. If the fourth ventricle and aqueduct are completely filled by the tumor, differentiation from other cerebellar tumors becomes impossible. A small tumor obstructing the foramen of Magendie may permit complete visualization of the dated fourth ventricle without producing any filling defect. The ventriculographic picture may then be indistinguishable from inflammatory obstruction of the foramen of Magendie.

## SUMMARY

Tumors of the cerebellum and the fourth ventricle produce such characteristic deformities that their exact location can, as a rule, be determined by technically perfect ventriculographic examination.

## REFERENCES

1. Journey, V. C., and List, C. F. Ventriculographic localization of intracranial tumors. II. mess of the aqueduct, pons and cerebellopontine angle. Am. J. ROENTGENOL. & RAD. Тневару, 1938, *40*, 348–356.

2. JOHNSCH, V. C., and LIST, C. F. Ventriculograpisc localization of intracranial tumors. I. Tumers involving the posterior part of the third ventacle and thalamus. Am. J. Roentgenol. &

RAD. THERAPY, 1937, 38, 77-91.
3. H\*DGE, F. J., and Johnson, V. C. Reliability of orain tumor localization by roentgen methods. Am. J. Roentgenol. & Rad. Therapy, 1935, 33, 744-751.

- 4. Lyshow, E., Ebenius, B., Lindblom, K., and SAHLETEDT, H. Das Ventrikulogramm, III. Teil Dritter und vierter Ventrikel. (Acta radid., Suppl. xxvi.) P. A. Norstedt & Söner, Stockholm, 1935.
- 5. McConnell, L. H., and Childe, A. E. Pneumograçãic localization of tumors of the brain. Arch Neurol. & Psychiat., 1937, 37, 33-55.



# THE INCIDENCE OF HYPEROSTOSIS FRONTALIS INTERNA IN FEMALE PATIENTS ADMITTED TO A MENTAL HOSPITAL\*

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INTEREST in a condition called "hyperostosis frontalis interna" was revived by Sherwood Moore<sup>4</sup> in a paper published in September, 1935. In this article Moore gave a comprehensive review of the literature on the subject and yielded to Morel<sup>6</sup> the credit of having introduced the name and of having made the first report of a living example of the condition.

Prior to the publication of Moore's article there was a considerable literature on the anatomy and pathology of the condition, where it was described under various names, but the first clinical description was that of Morel in 1930. Thus, he reintroduced to medical literature a subject which had been a dormant issue for many decades but he described it as one component of a clinical syndrome, since known as Morel's syndrome. This consisted principally of frontal bone hyperostosis associated with obesity, headache, neurological disturbance and a tendency to mental disorder. Since that time there have been numerous reports of individual cases which have usually presented all, or most, of these factors.

Moore's bibliography included reports of studies made on autopsy and museum specimens of varying types of groups, with a total of 65. It also included reports of 3 living cases. The authors quoted were Morgagni,<sup>7</sup> Casati,<sup>1</sup> Stewart,<sup>9</sup> Greig,<sup>2</sup> Morel,<sup>6</sup> van Bogaert,<sup>10</sup> Schiff and Trelles.<sup>8</sup> Moore's personal report was made from the study of the roentgenograms of approximately six thousand skulls of patients from general hospitals and clinics in St. Louis, Missouri.

In this large group he found 72 skulls which showed the presence of a hyperostosis of the inner table of the frontal bone, an

incidence of 1.2 per cent. In a later article<sup>5</sup> published in 1936, Moore reported the examination of the skulls of 695 additional patients among whom was a group of 33 femalez suffering with psychoses. He found 24 acditional examples of localized frontal hyperostosis in this second study, 14 of which occurred in the psychotic group. This gave an incidence of 1.41 per cent for the combined groups of the two studies.

In his 1936 report Moore also described several other more or less similar conditions of the skull. The whole communication was offered under a title which signified that all of these conditions are manifestations of a metabolic craniopathy. He stated that the surest method of making a diagnosis of any of these conditions was by means of roent-genographic examination.

It seemed to us that the most striking feature of Moore's later report was the fact that in a group of 33 psychotic females he found the condition in 14 instances, which was a strikingly high incidence, 42.4 per cent, as compared with the low incidence of 1.22 per cent in his original communication based on 6,000 cases taken from the general population. We wondered at his lack of comment on this feature of the situation. We were led to believe that this curious circumstance was worthy of further investigation.

In view of this and of the many references in the literature to psychotic and neurologic manifestations in these patients, we decided to carry out routine roentgenographic examinations of the skulls of female patients consecutively admitted to St. Elizabeth's Hospital, an institution for the care and treatment of mental disease.

<sup>\*</sup> Read before the Mid-Winter Conference of Eastern Radiologists, Washington, D. C., Feb. 10-11, 1939.

In carrying out this plan no selection of patients was made and the group included both white and colored females ranging in age from twenty-three to eighty-seven years, drawn from the civilian population of the District of Columbia. In each instance lateral and posteroanterior views were taken and in many instances the films were made stereoscopically. The group finally studied consisted of 200 patients.

We accepted the description of Moore as the criterion by which to judge the presence of the condition roentgenographically, and a group of four of us examined all flms together, no case being accepted unless a positive diagnosis was concurred in unanimously. In the group of 200 cases examined 50 unquestionably presented the condition here discussed. This is an incidence of 25 per cent. The accompanying illustrations show reproductions of typical films.

The next step in the investigation was to examine the histories and reports of both

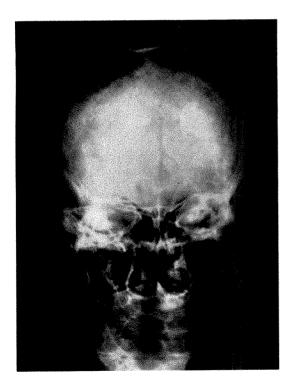


Fig. 1. Posteroanterior view of skull showing typical nodular form of hyperostosis frontalis interna.



Fig. .. Lazeral view of skull of typical case of noduar form of hyperostosis frontalis interna.

physical and mental examinations in each of the positive cases. In each instance the following factors were given special attention: age, color, mental diagnosis, serology, mer stread history, marital status, pregnancies, headaches, visual defects, obesity and neurological disorders.

The ratio of white to colored women was found to be approximately the same as that in the total hospital female population and there was no correlation between the presence of the hyperostosis and the menstrual history. There were 35 married and 15 single women. The former had a history of 72 pregnancies, or about 2 per individual. The incidence in age groups showed the greatest number to have been in the fifth decade of life. Table 1 shows the incidence in the age groups by decades.

Table I
INCIDENCE OF HYPEROSTOSIS FRONTALIS INTERNA
IN AGE GROUPS, BY DECADES

Age	Number of Positive Cases
20-29	6
39-39	8
49-49	10
50-59	9
60-69	9
70-79	4
80-89	4
	50

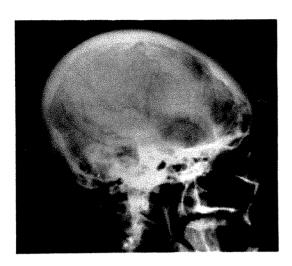


Fig. 3. Lateral view of skull showing a modified form of senile type of hyperostosis frontalis internal.

It appears that although 72 per cent of the cases occurred after the fortieth year of ife, nevertheless, contrary to the impression gained from the literature, a considerable proportion, 28 per cent, of the cases occurred in the earlier years. Ten per cent of the cases had a positive blood Kolmer relaction, which is approximately the same ratio as that found in the general mental hospital population, and presumably had no bearing on the situation.

TABLE II
INCIDENCE RELATIONSHIP OF MENTAL DIAGNOSIS
TO HYPEROSTOSIS FRONTALIS INTERNA

Mental Diagnosis	Number of Positive Cases
Dementia precox, hebephrenic	1 1
Dementia precox, catatonic	4
Dementia precox, paranoid	5
Psychosis with cereb, arteriosclerosis	1 1
Senile psychosis	4
Involutional psychosis	2
Manic depressive psychosis	5
Paranoid state	2
Psychosis with somatic disease	1
Psychosis with syphilitic meningo-en	-
cephalitis (paresis)	2
Epilepsy	1
Mental deficiency	I
Undiagnosed psychosis	1
A P	
	50

In reviewing the cases in a search for the factors usually alleged to constitute the syndrome, namely, obesity, headache, visual defect and neurological disorder, we found that obesity occurred in only 8 cases, or 15 per cent, and in none of these was the obesity of a type suggesting a definite endocrine disorder. Visual defects, except those due to trauma or senescence, were not present in any case. Headache was a basis of complaint in only 3 cases and neurological disorders, except those associated with epilepsy and paresis, were absent in all but one case and this case exhibited impaired hearing only.

In the light of the above observations it is impossible for us to concur in the opinion that a definite syndrome, sometimes referred to as the "triad of Morel," is present in cases of localized hyperostosis of the frontal bone, at least so far as the female population of a mental hospital is concerned.

A study of the incidence relationship to the mental diagnoses of these 50 cases is summarized in Table 11. It will be seen that

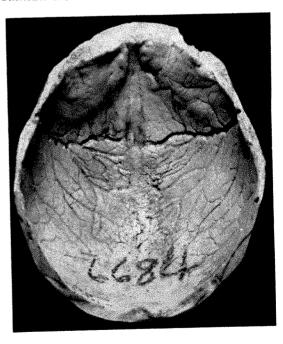


Fig. 4. Specimen from autopsy showing localized thickening of inner table of frontal bone with obliteration of intertabular space.

of the twenty-two types of psychoses classified by the American Psychiatric Association, thirteen are represented in this group of cases. These particular types are those of most frequent occurrence and constitute the majority of all cases of psychoses. Furthermore, it is of interest to note the fact that the largest number of cases in this study occur in two types of psychoses which usually predominate in a mental hospital, namely the dementia precox and the senescent-arteriosclerotic groups.

It therefore appears obvious that the occurrence of hyperostosis frontalis interna does not have any close or significant relationship to any one particular mental disorder.

Many hypotheses have been suggested as bearing on the etiology of frontal bone hyperostosis. Greig² in 1928 offered the suggestion that disuse absorption of calcium from other parts of the body in excess of the excretory powers resulted in the excess being deposited in the frontal region as an innocuous relief of a system saturated with calcium, an area which age renders least important. Moore⁵ more recently advanced the idea that it is the result of some metabolic disturbance bearing chiefly on a special calcium metabolism in the female. Henschen³ considered it merely a very frequent tertiary sex characteristic.

We have nothing to add to these speculations in regard to etiology but we believe that the condition is one which merits further extensive investigation, in both the general population and in the special population of mental hospitals. To us the most significant fact observed in our group of cases is that the localized condition called hyperostosis frontalis interna occurs about twenty times as frequently in females admitted, with mental disease, to a mental hospital as it occurs in the general population.

We therefore feel justified in regarding it as a broad, general, common factor occurring in many types of mental disease. Of what significance this is and whether or not it is related in any way to etiological fac-

tors of mental disease is a question of considerable interest to us but one for which we have no answer.

#### SUMMARY

A roentgenographic study was made of the skulls of 200 female patients consecutively admitted, with mental disease, to a mental hospital.

In this group, 50 cases, or 25 per cent, were found to present localized thickening and recreased density of the inner table of the frontal bone, a condition termed hyperostosis frontalis interna.

It is a noteworthy fact that this incidence is twenty times as great as that found in the general population.

Clinical examination and personal history of our cases did not show any occurrence of the syndrome described by Morel and noted by many other authors.

#### REFERENCES

- 1. Casatt, A. Die senilin Schädelveränderungen im Röntgenbild. Fortschr. a. d. Geb. U. Röntgen-trailen, 1926, 34, 335-342.
- 2. GREIG, D. M. On intracranial osteophytes. Edinburgh M. J., 1928, 35, 165-192; 237-260.
- 3. Henschen, F. Ueber die verschiedenen Formen von Hyperostose des Schädelachs. Acta path. 21 merobiol. Scandinav., Supp. 37, 1938, 236-246
- 4. More, S. Hyperostosis frontalis interna. Surg., Synec. & Obst., 1935, 61, 345-362.
- 5. Moore, S. Metabolic craniopathy. Am. J. Floentgenol. & Rad. Therapy, 1936, 35,
- 6. Morei, F. L'hyperostose frontale interne.

  Syndreme de l'hyperostose frontale interne
  avec adipose et troubles cérébraux. Gaston
  Don et Cie, Paris, 1930.
- 7. Mcreagni. De sedibus et causis morborum.
- 8. SCHOE, P., and TRELLES, J. O. Syndrome de Stewart-Morel (hyperostose frontale interne avec adipose et trouble mentaux), d'origine traumatique. *Encéphale*, 1931, 26, 768-779.
- 9. STEWART, R. M. Localized cranial hyperostosis in the insane. J. Neurol. & Psychopath., 1928, 8, 321-331.
- 10. TAN BOGAERT, L. Le syndrome de l'hyperostose frontale interne chez une malade présentant par ailleurs une cecité psychique par hemianopsie double. J. de neurol. et de psychiat., 1930, 30, 502.

# PERSISTENT FIBRIN BODY

# A PROBLEM IN DIAGNOSIS\*

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ALTHOUGH pleural effusions are common accompaniments of artificial pneumothorax, a residual fibrinous mass, or "fibrin body," occurs but rarely. Sachs¹ found 2 occurrences in 700 cases of pneumothorax. Hager and Langebeckmann² discovered only 1 in 400 cases. Mende³ found 3 in 512 cases. Zavod⁴ reported 5 cases, 1 of which was confirmed by autopsy. Out of 328 cases at the Sanatorium of the Jewish Consumptives' Relief Society, 1 developed

can easily be identified, but only by roentgenological examination. It has a spheroidal configuration of variable size, generally rests on the diaphragm, and is usually freely movable in the pleural space when pneumothorax is present (Fig. 1, A and B). The mass may increase in diameter by additions of fibrin from subsequent effusions. On the contrary, it has on occasion beer known to disappear after an effusion. Usually, with the re-expansion of the lung,

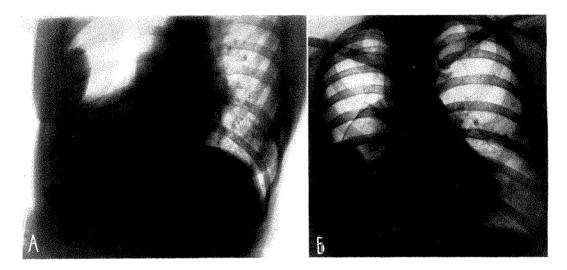


Fig. 1. A, fibrin body, ovoid in shape, resting in the right pmeumothorax cavity at the costophrenic angle. Right lung is almost completely collapsed. B, same fibrin body. The right lung is re-expanding.

a fibrin body during residence, and 3 were admitted with this sequel.

When this residuum follows a hydropneumothorax, it is usually produced by a massive serous, or more likely, a sanguineous effusion, although this is not the rule. Even a small effusion may result in this formation. The sanguineous type may be more conducive to fibrin body formation in that the fibrin content is greater. The "fibrin body" has certain characteristics and these foreign bodies are in some way absorbed and disappear completely. Zavod, however, states that they may persist roentgenologically for a period of four weeks to feur years. As a rule, they produce no symptoms, but in the case reported there was a constant dull ache over the left lateral chest wall, apparently due to pressure.

The case presented was intriguing because the persistence of the fibrin body after re-expansion of the lung led to a

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roentgen-ray configuration of considerable diagnostic interest.

# REPORT OF CASE

L. W., female, aged thirty-nine, was admitted to the Laurel Beach Sanatorium at Seattle, Washington, on April 3, 1937. The onset of pulmonary tuberculosis was pleuritic in 1935. On entrance to that institution cough, expectoration, weakness and streaking were found to be the cardinal symptoms. Examination there revealed a moderately advanced

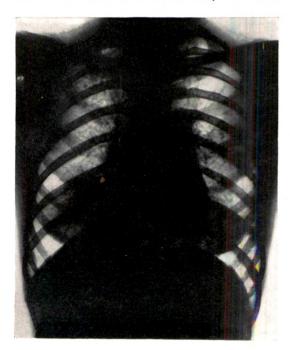


Fig. 2. Before pneumothorax—a moderately advanced bilateral infiltrative lesion.

infiltrative lesion involving both lungs (Fig. 2). Sputum was positive. A left artificial pneumothorax was instituted on May 15, 1937, because of hemoptysis, and discontinued six weeks later on account of adhesions (Fig. 3) and a complicating effusion (Fig. 4). Patient left on December 12, 1937.

She was admitted to the Sanatorium of the Jewish Consumptives' Relief Society on December 14, 1938, in an extremely emaciated condition. Cough was severe, and was daily productive of 2 ounces of sputum, which was positive. Her weight of 77 pounds was 55 pounds below standard. Examination revealed a small exudative lesion in the right upper lobe,

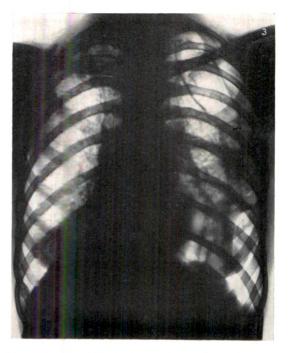


Fig. 3. Left artificial pneumothorax. Lung between the second and fifth costal cartilages is adherent to the ateral chest wall. Small amount of fluid in the costaphrenic angle.

with probable cavitation in the apex. In addition she had findings of increased left cardiac dullness and dullness at the left base. Roent-

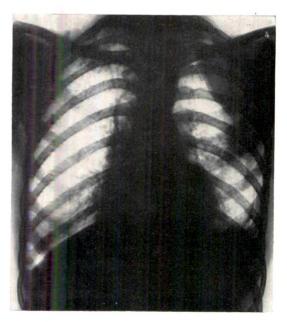


Fig. 4. Shows a left hydropheumothorax; formation of the fibrin body was preceded by an effusion.

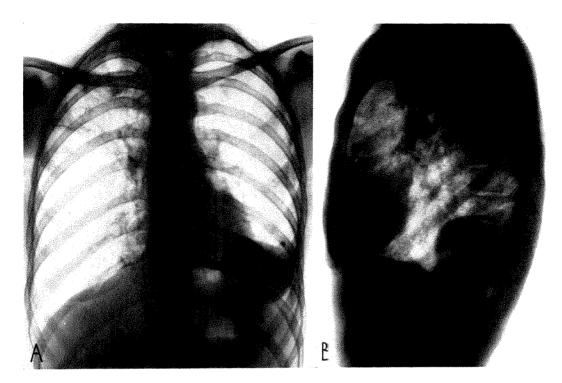


Fig. 5. A, exudative lesion of the right upper lobe with probable cavitation. There is a spheriodal mass about 3 inches in diameter, situated off the left heart border and resting on the diaphragm. The mass is sharply outlined and uniformly opaque. B, lateral view of fibrin body apparently attached to the left lateral chest wall.

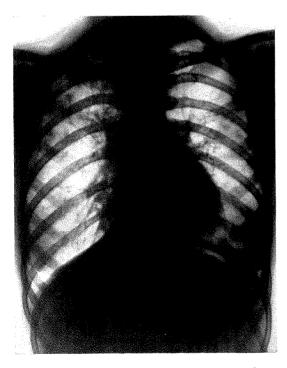


Fig. 6. Roentgenogram of March 21, 1939, almost complete disappearance of the fibria body.

genologically there was a spherical mass about 3 inches in diameter situated on the left diaphragm, posteriorly to the breast. The mass was sharply outlined, apparently attached to the left lateral chest wall, and uniformly opaque (Fig. 5,  $\mathcal{A}$  and  $\mathcal{B}$ ).

A problem in diagnosis with regard to the nature of the mass presented itself. Fibrin body, calcified lung abscess, xanthoma, adenocarcinoma of the lung, dermoid cyst, and echinococcus cyst were among the various considerations. A left artificial pneumothorax was attempted as a diagnostic measure but there was no free pleural space.

Subsequently, the previous history and roentgenograms were obtained from the Laurel Beach Sanatorium, Seattle. These revealed that the mass had not been present prior to the induction of pneumothorax (Fig. 2) and that its evolution was preceded by an effusion (Fig. 4). It could now be interpreted as a persisting fibrin body (Fig. 5, A and B). The last roentgenogram of March 21, 1939 (Fig. 6) shows the fibrin body almost completely absorbed.

# CONCLUSIONS

1. A fibrin body may occur as a harmless sequel of hydropneumothorax and can be diagnosed only by roentgen examination.

2. A case is reported of a pleural foreign body persisting two years after the discontinuation of pneumothorax; the roentgenological appearance of the mass without a coexisting pneumothorax space led to an interesting diagnostic problem.

3. The supposition that these fibrin bodies disappear promptly with the re-expansion of the lung is erroneous and might lead to false conclusions.

I am indebted to Dr. Frederick Slyfield of the Laurel Beach Sanatorium, Seattle, Washington, for his kindness in submitting to me the valuable roent-genograms in the above case (Figs. 2, 3 and 4).

## REFERENCES

- I. SACES, W. Blutfibrinkugeln im Pneumothorax-raum. Ztschr. f. Tuberk., 1928, 49, 354.
- 2. HAGER. E., and LANGEBECKMANN, F. Beobachtung Legeliger Gebilde im Pneumothoraxraum.

  Zisch. J. Tuberk., 1931, 63, 90-97.
- 3. Mende, P. Freie Körper in der Pleurahöhle. Beitr. z. Klin. d. Tuberk., 1927, 66, 293-296.
- 4. ZAVDC, W. A. Fibrin bodies in the pleural space in a case of artificial pneumothorax. Am. Rev. Tubre. 1936, 33, 48-54.



# CARCINOMA AS A COMPLICATION OF ACHALASIA OF THE CARDIA\*

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ONE of the most interesting and fascinating lesions of the alimentary tract is the condition commonly referred to as cardiospasm; interesting because of its controversial etiology, fascinating because of its spectacular clinical and roentgenological manifestations. For this lesion Walton has given the following definition: "A condition of dilatation and hypertrophy of the esophagus where, on post-mortem examination, no obstruction can be found distal to the dilatation."

When writing on this subject one is immediately confronted with the problem of a name. It has been referred to by so many names that there is now a long list of synonyms, such as idiopathic dilatation of the esophagus, hiatal esophagismus, primary dilatation of the esophagus, esophagectasia, cardiospasm, idiopathic hypertrophy of the esophagus, phrenospasm, preventriculosis and achalasia of the cardia. In this country the condition is most popularly known as cardiospasm, given preference no doubt because of its brevity as well as a misconception regarding its etiology. However, to one not familiar with this affection the name cardiospasm is misleading since it has been amply demonstrated by many investigators that there is no actual spasm of the cardiac orifice of the stomach. Furthermore, the term would seem undesirable since a true cardiospasm does occur but does not give rise to the pathological changes found in the condition under discussion. It seems reasonable to suppose that the cardiac orifice may become spastic as the result of local irritation or reflexly from pathological changes at a distance. Thus it is believed that fissures, ulcers or inflammatory changes in the lower end of the esophagus or fundus of the stomach

may result in spasm of the cardia as occurs at the pylorus, the ileocecal region or anal sphincter. Likewise, it is thought that gross intra-abdominal lesions such as gall-blacder disease may reflexly produce spasm of the cardia. Thus, it would seem necessary to differentiate between a true cardiospasm and the condition which we prefer to call achalasia of the cardia.

In using the term achalasia of the cardia we have chosen to follow the concept of Hurst regarding the pathogenesis of this condition. This concept has its inception in the physiological investigations of Kronecker and Meltzer who in 1883 showed that "every act of swallowing easily opens the cardia by reflex action." Accordingly, Einhorn, in 1888, describing a case of marked dilatation of the esophagus, concluded that it was due to "a lack in the reflez relaxation or opening of the cardia during the act of swallowing." This theory was lost sight of until Rolleston in 1896 made a similar suggestion. However, again this idea was given slight attention until Hurst, in 1913, quite independently brought forth the same theory. On the suggestion of Sir Cooper Perry the term 'azhalasia' meaning "absence of relaxaticn" was introduced by Hurst in 1915.

While this concept gives us a name and a mechanism of production of the changes as observed clinically it still leaves unsolved the matter of etiology. Believing that the primary affection responsible for the condition was to be found in the nervous system, Hurst in 1924 suggested that "the majority of cases... are caused by progressive organic disease involving Auerbach's plexus." This nerve plexus had been more or less neglected in previous studies of this condition. In early cases of achalasia

<sup>\*</sup> From the Departments of Radiology of the Jefferson Medical Col ege Hospital and the Graduate Hospital of the University of Pennsylvania, Philadelphia, Pa. Read at the Thirty-ninth Annual Meeing, American Roentgen Ray Society, Atlantic City, N. J., Sept. 19-22, 1938.

of the cardia there is only a compensatory hypertrophy of the esophagus, while dilatation occurs only after compensation fails. . Studying these early cases pathologically, Rake found lesions of a subacute inflammatory nature involving Auerbach's plexus, the changes being most marked at the cardia. In advanced cases with dilatation, the plexus and surrounding tissues were converted into a dense fibrous scar with a complete disappearance of the ganglion cells. These changes he believed are responsible for the failure of relaxation of the cardia although what initiates the alterations in the nerve plexus is apparently still unknown. The finding of inflammatory changes in Auerbach's plexus suggests that the lesion is an acquired one, yet there is much to lead one to suspect, as several writers have suggested, that it is of congenital origin.

Jackson would place the blame for this condition on the diaphragm, describing a diaphragmatic pinchcock, along with kinking of the abdominal esophagus as the normal mechanism by which food in the stomach is prevented from regurgitating back into the esophagus. Accordingly it is the failure of the diaphragmatic pinchcock to open normally that constitutes the stenosis in so-called cardiospasm.

It is not the purpose of this communication to deal with the etiology of this condition. Among the numerous theories that have been proposed only those of Hurst and Jackson have been mentioned since the concept of an achalasia appeals to us as being the most probable immediate cause of the condition. There most certainly seems to be an "absence of relaxation" of something or other, whether of the cardia or the diaphragmatic pinchcock we are in no position to say, although we rather favor Hurst's idea that the abdominal esophagus and a short section above the diaphragm is a true sphincter. This would harmonize with our own frequent roentgenological observation that the obstruction in achalasia of the cardia is sometimes above and sometimes below the diaphragm.

Efore proceeding with our justification for this presentation we are prompted by cus on and habit to give the "firsts" of the sub ect Most of the present-day literature mertions Purton, 1821, as the first to descripe a case of dilatation of the esophagus without obstruction, although Hannay who published an account of a case in 1833 is generally credited with having been first to recenize the condition. This would make our acquaintance with achalasia of the carcia of fairly recent origin which would be strange indeed considering the very striking clinical manifestations of this condition. It seems more probable that the affector, as a clinical entity, was known even in the earliest days of Medicine. We are ndbted to Dr. H. I. Goldstein who has called cur attention to a recorded account of the condition which dates back to 1679 when Thomas Willis published his Pharmaceutice Rationalis in which he describes a case of persistent vomiting, the clinical marifestations being typically those of achalasa of the cardia. Willis kept his patien alive and well for at least fifteen years by means of an instrument he devised for passage through the esophagus into the stomach, described as "a Rod, of a whale Bone, with a little round Button of Sponge fixed to the top of it." An improvised bougie which served an excellent purpose. The concluding remark of Willis is of interest in connection with the present consideration of carcinoma as a complication of achalasia of the cardia. To quote: "Without doubt in this case the Mouth of the Stomach being always closed, either by Tumour or Palsie. nothing could be admitted into the Ventricle unless it were violently opened." This very interesting account is to be found in Major's "Classic Descriptions of Disease." Return ag to more recent activities we find that in 1895 Rosenheim first examined a case with the esophagoscope and in 1897 Rumpelfirst used the roentgen ray in studying this condition.

We are also tempted to mention certain facts of general interest with which we were unfamiliar before making the present inves-

tigation, although they are not directly related to the matter at hand. Regarding the sex incidence we find that the condition is somewhat more frequent in men than in women. This does not coincide with our own somewhat limited experience. Furthermore, the affection is not peculiar to young neurotic females and has nothing whatever to do with psychoneurosis. Also of interest is the fact that salivation is a common complaint and results in considerable hypertrophy of the salivary glands.

Judging from reported cases, carcinoma as a complication of achalasia of the cardia is of rather uncommon occurrence, although Walton mentions Gottstein as stating that unless cured by treatment this complication frequently develops. In Gottstein's series of 33 cases there were 3 carcinomas. It is of interest that in one of the earliest cases to be reported there was an epithelioma. This case reported by Fagge was a man who, dying at the age of eightyfour, had complained of difficulty in swallowing for forty years. His symptoms were characteristic of achalasia of the cardia. At postmortem examination the only abnormal findings were in the esophagus which contained an epithelioma near its lower end. Apparently this was the cause of the patient's death. Below the growth the esophagus, for several inches extending down to and including the cardia, was markedly narrowed. The rest of the esophagus was considerably dilated and hypertrophied. Fagge considered the lesion a congenital stenosis of the lower end of the esophagus and this phase of the case interested him more than did the epithelioma occurring as a complication, as well it might.

Plummer, reporting a series of 301 cases, lists as associated conditions syphilis and psychoneurosis but makes no mention of carcinoma. One of his patients, however, died of a carcinoma of the esophagus eight months after treatment for achalasia of the cardia. Plummer states that in this case the diagnosis of achalasia may be questioned but the patient had had symptoms for five

to six years which along with the roentgenological manifestations were characteristic of achalasia. Furthermore, after dilatation the patient was relieved of her. dysphagia and had no further difficulty when last heard from which was two months before her death.

Vinson, reporting on the treatment of 683 cases of achalasia of the cardia, makes no mention of carcinoma as a complication. A report dealing specifically with epithelioma in association with achalasia of the cardia was made in 1931 by Rake who found 3 malignancies in 15 pathological specinens of this condition examined by him. He discusses the pathology of the condition and the basis for the development of carcinoma.

When one inquires into the pathology of acha asia of the cardia it is somewhat surprising that cancer as a complication is not of more frequent occurrence. It is no doubt true that some of these cases are being overlooked, but with the increasing frequency of postmortem examinations and the more universal employment of the esophagoscope it seems unlikely that any large number of cases are being missed. While we have not tabulated the actual number of cases of achalasia of the cardia that we have examined roentgenologically our experience no doubt is similar to that of hundreds of other roentgenologists working in a large city hospital. During this experience we have encountered 2 cases of carcinoma in association with achalasia of the cardia, and these form the basis of this

Significant in the pathology of uncomplicated cases of achalasia of the cardia is the absence of any organic obstruction at the lower end of the esophagus and yet roentgenologically the evidence of obstruction is the outstanding manifestation. As the result of the functional obstruction produced by failure of relaxation there occurs a state of hyperperistalsis of the thoracic esophagus whenever food or liquids are ingested. In consequence, over a period of years the thoracic esophagus shows evi-

dence of muscular hypertrophy, a compensatory mechanism. As long as this compensation is maintained no symptoms are produced, the patient is unaware of the condition, and in this early stage the lesion apparently cannot be diagnosed clinically. Whether any roentgenological manifestations are present at this stage of the disease that would enable one to recognize the condition is questionable. After muscular hypertrophy has reached a maximum and compensation begins to fail, dilatation of the esophagus occurs and this increases throughout the subsequent course of the disease unless checked by appropriate treatment. Eventually the entire thoracic esophagus becomes dilated and with this extreme involvement it becomes elongated and tortuous. Apparently the cervical esophagus never becomes much involved. We have on repeated occasions attempted to completely fill the esophagus with an opaque medium up to the hypopharynx but never with success. According to Hurst, when the esophageal contents form a col-

umn 8 inches high the cardia opens, per-

mitting some of the material to enter the stomach. Presumably the weight of the

contents is then sufficient to overcome the

obstruction offered by the cardia. The pa-

tient soon learns the necessity of taking in

a certain amount of food or liquids in order

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to have any enter the stomach. With the onset of dilatation the beginning of stagnation of esophageal contents occurs. This is at first intermittent but with progression of the disease there comes a time when the esophagus is never completely empty. The onset of stagnation initiates the period of secondary changes in the esophageal wall. Acting as an irritant the decomposing food produces inflammatory changes in the esophageal mucosa, giving rise to an esophagitis. The mucosa becomes flattened and smooth and subsequently ulcerated. The submucosa becomes greatly thickened but fibrosis with constriction apparently does not occur. These inflammatory changes may give rise to a true cardiospasm which is thus superimposed upon the achalasia. No doubt this is responsible for the conflicting statements that appear in the literature regarding the nature of the obstruction at the cardia and is probably also responsible for the name of cardiospasm being applied to this condition.

The ulcers which occur secondarily are usually shallow in character but occasionally they may penetrate with subsequent perferation of the esophagus. Ulceration may become so extensive that eventually nearly the entire mucosa may be destroyed. Numerous small islands of epithelium usually remain, however, and these under constant irritation from the decomposing esophageal contents undergo a hyperplasia resulting in small wart-like nodules or papillomata. These may subsequently become malignant and the occurrence of carcinoma in association with achalasia of the carda no doubt is on this basis. The extent of the secondary changes is dependent upon the height of the stagnant esophageal contents. Since these secondary changes are apparently an invariable accompaniment of the advanced stages of the disease it is indeed surprising that malignant change is not more frequently encountered.

The diagnosis of achalasia of the cardia is in the majority of cases relatively simple. Since symptoms do not appear until dilatation of the esophagus occurs and since this dilatation may be expected to proceed rather slowly one may anticipate that the onset of the clinical manifestations will be insidious. When the patient's complaints have become sufficient to cause him to seek medical attention one may be assured that the disease is of some duration and well established. The history, therefore, is usually one of increasing difficulty in swallowing over a period of years although occasionally the onset is quite abrupt. Dysphagia is intermittent at first but subsequently becomes more or less constant. While this is the outstanding symptom there are others which serve to produce a definite clinical picture. Regurgitation is a fairly constant one. Actual vomiting does not occur and

there is no nausea or retching. The regurgitated material contains unchanged food, much mucus and no free hydrochloric acid. Substernal pain is often present and may at times be the predominant complaint. Certain respiratory symptoms such as cough and dyspnea after eating may be complained of. Excessive salivation may be a distressing symptom. This combination of clinical manifestations are such as to lead one to suspect the existence of an achalasia of the cardia, but the diagnosis should be established by a roentgenologic examination, the passage of bougies and direct visualization through the esophagoscope.

Roentgenologically the typical case offers no diagnostic difficulties. When observed roentgenoscopically the obvious obstruction either at the level of the diaphragm or at the cardiac orifice with the marked dilatation of the thoracic esophagus produces a picture unlike anything else seen in the esophagus (Figs. 3 and 4). The lower esophagus ends abruptly presenting a smooth funnel-shaped contour or at times may be somewhat angulated. There is no irregular filling defect as seen in cancer. The dilatation varies considerably in different cases but is usually much greater than is encountered in any other type of obstructive lesion of the esophagus. When marked, there is noted considerable tortuosity which causes the esophagus to bulge to the right beyond the cardiac silhouette (Fig. 1). Usually the obstruction is complete so that none of the contents enters the stomach until the amount in the esophagus reaches a certain height when a thin stream of the opaque material will be seen entering the stomach. This feature is quite striking and is not to be observed in other esophageal lesions. The characteristic manner in which the opaque medium falls through the esophagus indicates the presence of a large amount of fluid and the mottled appearance presented by the dilated esophageal shadow is due to the presence of retained food. A distinct fluid level is often discernible located high in the thorax or in the lower part of the neck. In

the lateral view the enlarged esophagus tends to displace the trachea forward. This along with a fluid level may lead one to suspect the condition on the plain films of the chest (Fig. 2). This appearance is not, however, pathognomonic of achalasia since it is also seen in carcinoma of the esophagus, diverticulum and benign stenosis. In the lower part of the chest just above the diaphragm there will be noted a triangular shadow, apex directed upward. This is due to the shadow of the dilated fluid-filled esophagus superimposed upon the cardiac shadow. This appearance along with the displaced trachea and fluid level will probably not be found in any other esophageal condition.

Plummer warns against accepting the diagnosis of so-called cardiospasm on evidence presented by roentgenographic examination without considering all features of the case, and with this warning we are in hearty agreement. We believe the investigation of a case of achalasia of the cardia is not complete without a careful esophagoscopic examination. This is contrary to the statement made by Plummer in 1921 when he says that "an esophagoscopic examination in the majority of cases is quite unnecessary, knowledge obtained is usually not worth the effort," while Hurst and Rake writing in 1930 state that, "esophagoscopy is superfluous, as the diagnosis can be made with more certainty and much less unpleasantness by means of the x-rays." These are probably not the present-day views of authorities on this subject. Rake, discussing epithelioma in association with achalasia of the cardia in 1931 states that "frequent esophagoscopic examinations should be done to detect such changes early." The cases here reported testify as to the value of the esophagoscopic examination. There is no other way to detect the secondary changes occurring in the esophagus and certainly a knowledge of such changes is important in the proper management of a case of achalasia of the cardia.

The following case is quite characteristic

both clinically and roentgenologically of the typical case of achalasia of the cardia.

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CASE I. E. K., white female, aged fifty-five. This patient's chief complaint was vomiting in the evening when she lay down, accompanied by choking sensation. This symptom was more of a regurgitation than a true vomiting and she had complained of this intermittently for the past thirteen years. The material regurgitated was the food as it was ingested. There was considerable mucus present but never any blood. No pain but occasionally she complained of a sense of fullness beneath the sternum. Her food would seem to lodge somewhere in the chest. She has gradually lost weight since the onset of her symptoms and now she is quite weak. She appears fairly well nourished, however. She has been under the care of many physicians during the past thirteen years who have made varous diagnoses but none have ever suggested or requested a roentgen examination.

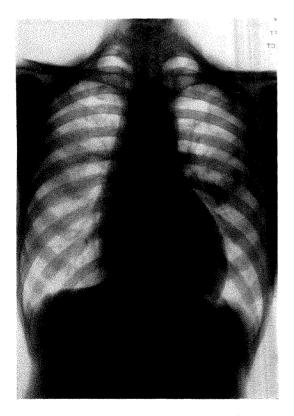


Fig. 1. Case 1. Chest in a case of achalasia of the cardia. What appears to be an enlargement of the heart to the right is actually the markedly dilated esophagus extending to the right as seen in Figure



Fig. 2. Case 1. Lateral view of chest. Note forward displacement of trachea and fluid level, also triangular standow just above the diaphragm due to the 1 lateral fluid-filled esophagus superimposed upon the heart.

Roerstzemslogic Examination. Examination of the chest showed what appeared to be considerable en argument of the heart to the right (Fig. 1). Subsequent examination revealed that the right borde of the cardiac shadow was actually due to a rankedly enlarged esophagus. In the lateral wie the trachea appeared to be displaced somewhat forward and there was a distinct fluid kevel seen in the esophagus (Fig. 2). The escenhagas visualized by the barium meal was encraously dilated (Fig. 3). There was a definite abstruction at the cardiac orifice of the stomach which was smooth and regular in contour (Fig. 4). There was a large non-opaque residue in the esophagus, which was quite tortuous. Canciagion: Marked degree of preventriculosis, with marked dilatation and tortuosity of the theracic esophagus. Esophagus projecting to the game side of the cardiac shadow.

Esopheges pic Examination. There was an enormous diletation of the entire thoracic esophagus with maiderable retention of fluid.



Fig. 3. Case I. Barium-filled esophagus shows marked dilatation and tortuosity.

This dilatation extended from the cardiac orifice up to the level of the suprasternal notch. The esophagus showed tight closure at the cardiac orifice but no difficulty was encountered in passing the instrument into the stomach. The mucosa of the dilated esophagus was markedly inflamed and presented numerous superficial erosions. *Esophagoscopic diagnosis:* Preventriculosis, so-called cardiospasm.

The one outstanding condition from which achalasia of the cardia must be differentiated is carcinoma involving the lower end of the esophagus. As a rule, the differentiation is not difficult either clinically or roentgenologically. Carcinoma usually occurs after forty years of age, is more frequent in men than in women, gives a relatively short history of difficulty in swallowing which becomes progressively worse and is accompanied by definite loss in weight. In achalasia of the cardia, on the contrary, the symptoms are often inter-

mittent in character and, as a rule, the general well being of the patient is in marked contrast to the patient with malignancy.

Roentgenologically the obstruction at the lower end of the esophagus is seldom complete. There is usually noted a continuous, much distorted stream of opaque material entering the stomach. The markedly irregular contour of the lesion is in sharp contrast to the smooth funnel-shaped appearance in achalasia of the cardia. While there is some dilatation of the esophagus proximal to the lesion this is seldom very marked. The patient takes the opaque meal a mouthful at a time and there is not the tendency to completely fill the esophagus as is so characteristic of patients with achalasia of the cardia.

While these clinical and roentgenological features readily distinguish the malignant lesion from achalasia, one occasionally encounters a case in which the two lesions

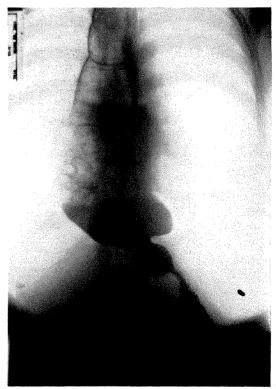


Fig. 4. Case I. Showing the characteristically smooth and regular funnel-shaped obstruction at the lower end of the esophagus in achalasia of the cardia.

may simulate each other. The following case is an example of this kind.

Case II. M. K., female, aged twenty-six. The patient's chief complaint was discomfort beneath the ensiform cartilage for the past seven months. She began to have difficulty in eating three months ago. This was characterized by a fullness beneath the sternum and a feeling as though the food stopped before it reached the stomach. She found if she drank liquids slowly she was able to retain it, but solid foods came up just as swallowed. Getting rid of the food gave relief. For the past few weeks she had had difficulty in taking water.

Contents removed from the esophagus consisted of milky material, saliva and no blood. The blood count showed a moderate secondary anemia. The Wassermann reaction was negative.

Roentgenologic examination (Figs. 5 and 6) was reported as follows: The bony framework

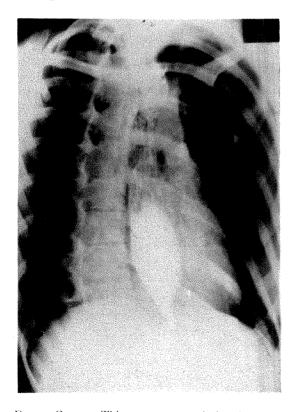


Fig. 5. Case II. This case presented the characteristic findings of achalasia of the cardia and was so diagnosed roentgenologically. Esophagoscopic examination revealed an organic stenosis of the lower end of the esophagus and at operation this was found to be due to an extensive malignancy.



Fig. 6. Case M. Lateral view of esophagus showing the appearance typical of an achalasia of the cardia in a case of cancer.

of the her is negative. Examination of the esophages howed a definite dilatation of the thoracic person, with an obstruction at the cardiac prifer of the stomach. The lower end of the employeus is smooth and regular in contour. The appearance is characteristic of a preventriculosis. We could demonstrate no organic lesion Conclusion: Preventriculosis of a moderate degree.

Esophegosepic Examination. The upper esophagus was normal. The thoracic esophagus showed or saferable dilatation with retention of fluid. The was no barium remaining in the esophagus at the time of the examination. The dilatation extended down to the level of the diaphragm. The abdominal esophagus was closed tigatly just below the level of the hiatus. The muchus membrane was very much reddened, the kened and granular in appearance. A No. 18 I later passed through the strictured area with sight resistance. It was not thought advisable or move tissue for biopsy. Esophagoscopic deagness: Organic stenosis of the hiatal esophagus. Neoplasm? Inflammatory? The

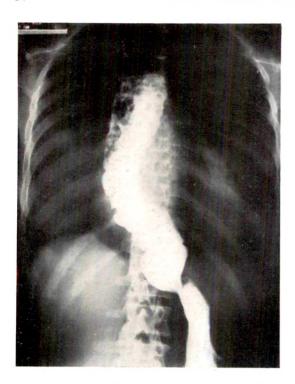


Fig. 7. Case III. At the first roentgenologic examination the usual findings of achalasia of the cardia were revealed. At this time the esophagus was filled with a large amount of fluid and retained food. This accounts for the mottled and irregular appearance of the esophageal shadow.

extent of the lesion and the poor condition of the patient would seem to justify a gastrostomy before further diagnostic studies are made.

At operation there was found an infiltrating cancer of the cardiac end of the stomach and esophagus. Metastasis to the liver, omentum and transverse colon. A gastrostomy was performed.

Comment. The age of the patient, twentysix, the clinical manifestations and the roentgenological findings were characteristically those of achalasia of the cardia. The esophagoscopic examination revealed the true nature of the lesion and led to the only form of therapy that offered the patient any relief from her symptoms.

Because of the grave prognosis in cancer of the esophagus, this condition should be uppermost in the mind of the roentgenologist when called upon to examine a patient whose chief complaint is dysphagia. One is inclined to be somewhat relieved when the

characteristic features of an achalasia of the cardia appear upon the fluoroscopic screen. With these findings the diagnostic problem is usually considered solved and one is not inclined to look for complicating lesions. The diagnosis of achalasia of the cardia also usually suffices for the clinician and treatment consisting, as a rule, of dilatation of the site of obstruction is proceeded with. If one bears in mind the pathology that occurs in the esophagus as the result of achalasia of the cardia the possibility of some complicating lesion would appear more probable and worth looking for. Because of the seriousness of a malignant condition the roentgenologist must make every effort to exclude this possibility when confronted by an achalasia of the cardia. The presence of such a complication can readily be missed as is illustrated by the following case.

Case III. T. M., white, female, aged forty-eight. The patient's chief complaint was pain in the abdomen. Onset of gastrointestinal upsets ten years ago at the death of her parents, with episodes of indigestion at ten and five years ago consisting of epigastric pain, nausea, vomiting and constipation. Fifty-seven pounds weight loss in ten years. An attack of "flu" five months ago with progressive downhill course characterized by dyspnea, swelling of ankles and weakness. Present digestive symptoms are of one month duration.

The blood showed a slight anemia with a slightly increased leukocyte count. Blood chemistry negative. Blood Wassermann negative. The stool was positive for occult blood.

Roentgenological examination (Fig. 7) showed the esophagus to be markedly distended from the neck to the hiatus. It was tortuous and at the dependent portion drooped. About an inch above the hiatus, the appearance on the posterior and left lateral surface suggested the presence of an ulcer. Small amounts of the barium meal were occasionally ejected into the stomach. The subdiaphragmatic portion of the esophagus was very narrow during these ejections. *Conclusion:* Esophagus—marked achalasia. We are not certain whether the point of constriction is above or below the diaphragm. We are inclined to think that it is above. The appearance suggestive of ulcer of



the esophagus near the point of constriction is probably due to mucosal folds, rather than ulcer.

Esophagoscopic Examination. The entire thoracic esophagus was enormously dilated. About 35 cm. from the upper teeth there was encountered a fungating mass the size of the end of the index finger, projecting internally from the right lateral esophageal wall. An ample specimen of tissue was removed. The lower portion of the esophagus was explored, the fungating mass producing no obstruction in the esophagus. About 44 cm. from the upper teeth there was encountered a closure of the hiatal esophagus typical in appearance of socalled cardiospasm or achalasia. The tube passed on into the stomach without undue resistance. There was no ulceration or infiltration noted as far as was examined. Esophagosepic diagnosis: Achalasia, so-called cardiospasm, with closure of the lower end of the esophazus. Fungating lesion in the mid-thoracic esophagus, cancer?

A second roentgen examination (Fig. 8) was then done after complete removal of the contents from the dilated esophagus with the following result: Patient was examined after aspiration of the esophagus with the knowledge that a neoplasm had been found by esophagoscopic examination. At this time a large penetrating ulcer was found about 4 inches above the cardia. There was also a filling defect in the esophagus at this level. We should conclude from the size of the ulcer and the presence of a filling defect that the lesion at this site in the esophagus was probably a malignant neoplasm and not a benign one. Conclusion: Probable cancer of the esophagus associated with achalasia.

The pathological report of the biopsy was "squamous cell carcinoma, Grade 3."

This case directs our attention to two important points. The first is that the roentgenologic examination in cases of achalasia of the cardia is not complete until examination has been done after the esophagus has been evacuated of its retained contents. At the first examination, the esophagus will usually contain a variable amount of residue. While this will not interfere with arriving at the diagnosis of achalasia of the cardia, the examination should be repeated after the esophagus has



Fig. 8. Case III. Second roentgen examination after esophague had been evacuated of its retained contents shows a lesion just above the cardia due to carcinom. This was missed at the first examination.

been empired in order to detect any complicating sions.

The second point is the importance of the esoph goscopic examination. As previously nontioned, no investigation of a case of actalasia of the cardia can be considered complete without direct visualization through the esophagoscope.

While one would anticipate that most of the malignant conditions associated with achalasia of the cardia would be located in the distal portion of the esophagus, this need not necessarily be the case. One must remember that secondary mucosal changes may be found in any portion of the dilated esophagus, and since the dilatation may involve the entire thoracic portion, one may expect to find malignant degeneration occurring relatively high. There is, of course, always the possibility of a carcinoma occurring quite independent of an existing achalasia. One must therefore be prepared to find a cancer in any part of the esopha-

al.

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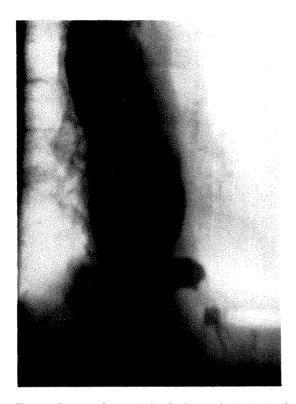


Fig. 9. Case iv. In 1926 the findings of achalasia of the cardia were confirmed by esophagoscopic examination. No complicating lesion was found at this time.

gus in association with an achalasia of the cardia, as is illustrated in the following case.

Case IV. F. S., white, male, aged forty-six. This patient was first seen in 1926 at the Jefferson Hospital at which time he was complaining of difficulty with lodgment of both liquid and solid foods, regurgitation and marked weight loss, 30 pounds. The onset was about eight years before with severe pain in the stomach and inability to retain food. One physician told him he had "autointoxication" while another treated him for gastric ulcer, with some improvement in his condition although regurgitation persisted. In 1925 he attended a hospital in another city where numerous studies were carried out and a diagnosis of cardiospasm was made.

Roentgenologic examination (Fig. 9) was carried out on November 30, 1926. There was a great dilatation of the esophagus. The obstruction was at the extreme lower end and was evidently spasmodic in character. The esophagus

evidently contained a considerable amount of fluid or food at the time of the examination.

At the esophagoscopic examination on December 2, 1926, the thoracic esophagus was found enormously dilated. The mucosa was inflammatory and hard masses of food were found adherent. There was no evidence of ulceration or erosion observed. The hiatal esophagus seemed normal in appearance and a 9 mm. standard esophagoscope was passed through the hiatus into the stomach without meeting any obstruction. *Diagnosis:* Preventriculosis, so-called cardiospasm.

During the course of the next two years the patient was treated by means of hydrostatic dilatation with much improvement in his condition.

The patient was next seen at the Graduate Hospital in 1936. He complained of essentially the same symptoms as before, with the exception that he now had a cough which was thought to be due to asthma. He has continued to subsist on liquid food but his weight has definitely dropped in the past year.

Roentgenologic examination of the chest (Fig. 10) on March 6, 1936 showed a marked

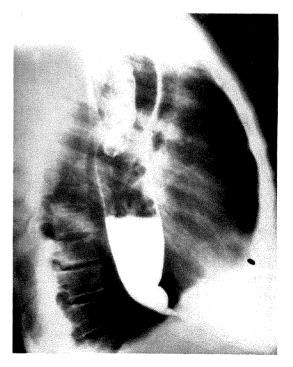


Fig. 10. Case IV. When examined in 1936 there was, in addition to the achalasia, a large carcinoma arising from the posterior wall of the upper thoracic esophagus.

degree of pulmonary emphysema. In the lateral view there was noted some anterior displacement of the trachea. Study of the esophagus revealed a hugely dilated, somewhat tortuous esophagus, the dilatation extending from the cardiac orifice of the stomach to the suprasternal notch. The appearance was typically that of a preventriculosis. Considerable amount of contents escaped from the esophagus into the stomach. In the upper portion of the theracic esophagus along the posterior wall involving a distance of approximately 4 inches, there was a large filling defect which encroached upon the lumen of the esophagus. This was very suggestive of a malignant lesion in this region. Conclusion: Marked pulmonary emphysema. Advanced preventriculosis. Large filling defect involving the posterior wall of the upper thoracic esophagus probably due to malignancy.

At the esophagoscopic examination on March 7, 1936, the upper esophagus was normal. At a point just below the level of the suprasternal notch there was encountered a huge fungating mass which rose from the posterior wall of the esophagus. It presented an ulcerating surface and had the typical appearance of extensive carcinoma of the esophagus. An ample specimen of tissue was removed for biopsy. Inspection of the lower end of the esophagus showed the typical appearance of preventriculosis. A small tube was passed into the stomach. The extent of the ulceration on the posterior wall of the esophagus as outlined by the roentgen ray was confirmed. Esophagoscopic diegnosis: Preventriculosis. Extensive carcinoma of the upper third of the thoracic esophagus.

Pathological report of biopsy was "squamous cell carcinoma."

The last 3 cases here reported emphasize the necessity of keeping constantly in mind the possibility of carcinoma when called upone to examine a patient whose symptoms are referred to the esophagus. The relationship of cancer to achalasia of the cardia is twofold. In the first place the differential diagnosis must be made between carcinoma of the lower end of the esophagus and achalasia of the cardia, and secondly one must exclude cancer as a complication in achalasia of the cardia. There is nothing in the symptoms or physical findings to lead one

to suspect an associated malignancy in a case of achalasia with the exception of the history of vomiting blood or the finding of occult blood in the stools which do not occur in uncomplicated cases of achalasia of the cardia. Therefore, a careful roentgenologic and esophagoscopic examination should constitute a part of the routine investigation of every case of achalasia of the cardia.

## REFERENCES

- 1. ABELL, I. Cardiospasm. Surg. Clin. North Amer-1030, 10, 897-899.
- 2. ARAEA, M. A., and HURST, A. F. Modern Aspects of Gastroenterology. William Wood & Ca., Baltimore, 1933.
- 3. SEATTIE, W. J. H. M. Achalasia of cardia. St. Bath. Hosp. Rep., 1931, 64, 39-84.
- 4. Einen, M. Case of dysphagia with dilatation of sesophagus. Med. Rec., 1888, 34, 751-753.
- FAGCE, C. H. Case of simple stenosis of esophagus followed by epithelioma. Guy's Hosp. Rep., 1872, 17, 413.
- Freeman, E. B. Etiology, pathology and symptomatology of chronic cardiospasm. South. M. 7., 1930, 23, 238-243.
- 7. HANEAY, A. J. Edinburgh M. & S. J., 1833, 40,
- 8. Hurst, A. F. Medical Essays and Addresses on Digestive and Nervous Diseases. Wm. Heinernæn, London, 1924.
- 9. Eurss, A. F. Treatment of achalasia of cardia (so-called "cardiospasm"); general considerations. Lancet, 1927, 1, 667.
- 10. MURST, A. F., and RAKE, G. W. Achalasia of cardia (so-called cardiospasm). Quart. J. Med., 1900, 23, 491-508.
- 11. Jackson, C. Diaphragmatic pinchcock in socalled "cardiospasm." Laryngoscope, 1922, 32, 135-142.
- 12. Eronecker, H., and Meltzer, S. Der Schluckmechanismus, seine Erregung und seine Hemmung. Arch. f. Physiol., 1883, Suppl. -Bd., 338– 362
- 13. MAJOR, R. H. Classic Descriptions of Disease. Charles C Thomas, Springfield, Ill., 1932.
- 14. McKenney, R. Cardiospasm with autopsy. Tr. Ana. Laryng. Ass., 1929, 51, 259.
- 15. MILLER, J. W. Case of severe cardiospasm mistaken and treated for carcinoma of esophagus. Largngoscope, 1931, 41, 780-782.
- 16. Mosher, H. P. The liver tunnel and cardiosomm. Laryngoscope, 1922, 32, 348-362.
- 17. FEMBERY, M. S., and RITCHIE, J. General Pathology. Longmans, Green & Co., New York, 1913.

- 18. Penn, H. S. Cardiospasm in cancer of the stom-
- ach. M. J. & Rec., 1933, 137, 490-494.
  19. Plummer, H. S., and Vinson, P. P. Cardiospasm; report of 301 cases. Med. Clin. North America, 1921, 5, 355.
- 20. PURTON, T. Lond. Med. & Phys. J., 1821, 46,
- 21. RAKE, G. W. Guy's Hosp. Rep., 1926, 76, 145.
- 22. RAKE, G. W. Pathology of achalasia of cardia. Guy's Hosp. Rep., 1927, 77, 141-150.
- 23. RAKE, G. W. Epithelioma of esophagus in association with achalasia of cardia. Lancet, 1931, 2, 682.

- 24. ROLLESTON, H. D. Simple dilatation of esophagus. Tr. Path. Soc., Lond., 1896, 47, 37.
- 25. ROLLESTON, H. D. Idiopathic dilatation of esophagus. Tr. Path. Soc., Lond., 1899, 50, 69.
- 26. Rosenheim, T. Deutsche med. Wchnschr., 1899,
- 25, 740; 756; 781. 27. Vinson, P. P. Treatment of cardiospasm. South. M. J., 1930, 23, 243-247.
- 28. Walton, A. J. Surgical treatment of cardiospasm. Brit. J. Surg., 1924-1925, 12, 701-737.
- 29. WILLIS, T. Of vomiting. Pharmaceutice rationalis, T. Dring, C. Harper & J. Leigh, London, 1679, p. 23.



out-patient department. One year later she was leading a very active life, and denied any abdominal symptoms. Roentgen studies show no change in the lung fields and no evidence of pneumoperitoneum. The erthrocyte sedimentation rate on March 20, 1938, was 24 mm. in the first hour.

## DISCUSSION

The source of the gas in the peritoneal cavity of this patient remains unexplained. When questioned she stated that she had not taken a vaginal douche "in over thirty years."

No history was obtained of gastrointestinal symptoms, trauma, diagnostic air injection, or anything which might indicate cause of this condition except a chronic sough. There was no evidence of peritonitia as judged by the clinical course, leukocyte count, temperature, or blood chemistry. The stool was guaiac negative and repeated astrointestinal examinations and barium gratrointestinal examinations and barium eremas disclosed normal findings.

The pneumoperitoneum persisted until ner nineteenth day in the hospital, i.e., wenty-one days after the onset of symp-

damage has been done. The mechanism of "sealed off" by some means before much tions of the gastrointestinal tract become It is undoubtedly true that some perforathat infection did not enter with the gas. endain this phenomenon it must be assumed with the absence of peritonitis. In order to age from any possible gastrointestinal source reconcile such prolonged or repeated leakthe pneumoperitoneum. It is difficult to reopened at intervals, in order to maintain trat the air inlet either remained open or raoperitoneum in our case seems to indicate The twenty-one day duration of the pneutollowing diagnostic pneumoperitoneum. c. of air is absorbed in four to eight days enced observers report that 1,000 to 4,000 teen carried out on humans, but experiimilarly accurate observations have not eighty hours per 100 cc. for pure nitrogen. mito young rabbits and found this to be absorption time of numerous gases injected Fühner in 1921 studied the peritoneal

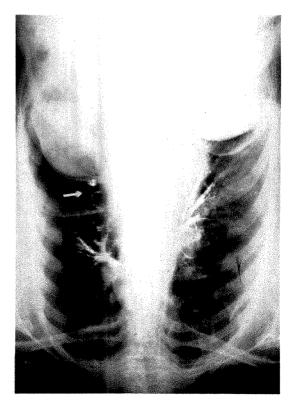


Fig. 3. Lipiodol study of the chest. The arrow points to a pocket of lipiodol which by lateral and stereoscopic films was seen to be in centract with the posterior slope of the high eff liaphragm. The pneumoperitoneum, which is seen nere on the eleventh day after onset of symmtoms, did not completely disappear until the twenty-lively disappear until the twenty-livel day.

lowermost portion of the left lower lobe. Stereoscopic films of the chest showed the pool of lipiodol to be in direct contacts with the abnormally high left disphragm. This was interpreted as an emphysemateur balla filled with the opaque material. No lipic col was seen with the opaque material. No lipic col was seen

The patient never became very all Her rectal temperature never exceeded 100° 3, her white cell count never exceeded 7,000 and she improved steadily with rest in bed this as of the chest one week after admission and of the same amount of pneumoperaturement which had been present on admission. Fines on the sixteenth hospital day still shewer, he presence of free intra-abdominal air, and the twenty-first completely disappear until the twenty-first day. She was entirely asymptomatic after the second week. On the twenty-second day she second week. On the twenty-second day she was discharged and has been followed in the was discharged and has been followed in the

Blood nonprotein nitrogen was 35 mg, per 100 cc., and the complete blood partition was normal. Erythrocytic sedimentation rate was 56 mm, in the first hour. Venous pressure was 65 mm, of water, the blood Wassermann negative and sputum contained no tubercle bacilli. No occult blood or other abnormalities could be found on repeated examination of the stools. Electrocardial damage and occasional premature contractions.

gastrium and over the lower part of the chest anteriorly on both sides. The pain awakened her about one o'clock at night. It was sharp and stabbing in character, was aggravated by breathing, and was not relieved by soda, aspirin or a heat pad.

The patient stated that she had a dry hacking cough for twelve or fifteen years. She was thought to have had pneumonia four and onehalf years previously, and for three years had noticed progressive dyspnea, substernal oppres-

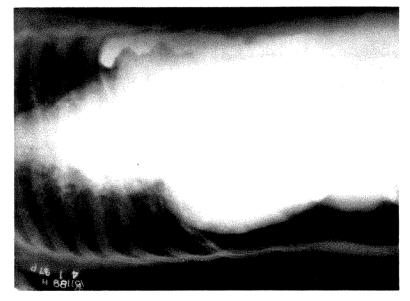


Fig. 2. Film of the abdomen taken with the patient lying on the left sade and the roentgen beam directed in a horizontal plane. The normal outlines of the lateral margin of the liver and kidney are clearly seen. The shadow of the right diaphragm is not well reproduced. The position of the descending colon is indicated by a small barium residue in it.

peculiar pooling of the opaque material in the chial tree and it was noted that there was a enemas. Lipiodol was instilled into the bronof the colon was found by repeated barium of the stomach or duodenum. No abnormality toms, disclosed no evidence of organic disease and nineteen days following the onset of sympintestinal examinations on two occasions, hve mothorax was sound (Figs. 1 and 2). Gastrothickened pleura in both apices, but no pneu-There was evidence of old fibrotic changes and sion. The heart was shifted slightly to the right. fith rib anteriorly, and was limited in excurphragm was very high, lying at the level of the phragmatic demes. The dome of the left diaa large amount of free air under both diaamination disdesed a pneumoperitoneum with Roentgenographic and roentgenoscopic ex-

sion and wheezing respirations in addition to

cell count was 7,000 with a normal differential. with 4,080,000 red blood corpuscles. The white plood studies showed 69 per cent hemoglob n tor evidence of generalized arteriosclerosis. mainder of the examination was negative except tender without spasm or rigidity. The releft base. The abdomen was distended and sounds on the left, with a few dry rales at the fremitus, hyperresonance and decreased breath the trachea to the right. There were absert tted expansion on the left and deviation of 130/68. Examination of the chest disclosed linand respiration were normal. Blood pressure not appear dangerously ill. Temperature, pulsz cyanotic and slightly dyspneic woman who did Physical examination disclosed a slightly the persistent cough.

this has been discussed by Warfield and others. Johnson measured a series of perforated peptic ulcers and found the average size to be 6.5 mm. while some were only mm. in diameter. It is easily conceivable that a small ulcer might perforate, allow considerable gas to escape, and become sealed off again without producing much peritoneal irritation. This is what wa termed "valvular pneumoperitoneum" by Singer. Even in such a case, however, i seems probable that necropsy, abdomina exploration, or satisfactory gastrointestina. examination by roentgen methods would disclose enough evidence to suggest the presence of an organic lesion if one existed

The pool of lipiodol contiguous to the diaphragm was interpreted as possibly be ing an emphysematous bulla filled with the opaque material. The possibility that the pneumoperitoneum was produced and maintained by air which passed through the diaphragm was discussed. Whether this was made possible by congenital weakness in the eventrated dome, coughing, mechanical erosion, rupture of an emphysematous bulla, some local inflammatory process, or leakage around the structures in the diaphragmatic hiati cannot be determined.

The intra-abdominal pressure is nearly always negative (Wagoner) and, according to Salkin, it may reach 50 mm. of water be low that of the atmosphere. The introduction of fluid or air into the peritoneal cavity does not raise the pressure sharply because of the "abdominal accommodation" described by Coombs. Therefore, if air should enter through an aperture in the diaphragm, one could not expect it to be expelled through the same route unless the intra-abdominal pressure became greatenthan that of the atmosphere.

The source of the gas and its mode of entry into the peritoneal cavity have not beer conclusively proved, but the patient's clinical course together with the lipiodo studies suggests the possibility that there might have been at least a temporary communication between the aerated lung parenchyma and the peritoneal cavity.

#### SHMMARY

Spontaneous pneumoperitoneum usually results from perforation of a viscus. Two cases have previously been reported in which no cause for the free gas within the abdomen could be found.

A case of spontaneous pneumoperitoneum, which lasted twenty-one days, in a woman, aged seventy, is reported. No evidence of peritonitis or of disease of a viscus was found. Lojiodol instilled into the bronchi disclosed what appeared to be a bulla in contact with the thin, eventrated left diaphragm. As no other explanation for the pneumoperitoneum could be found, the possibility that air may have entered the abdomen by passing from this bulla through the thin diaphragm is suggested.

I wish to express my sincere appreciation to Dr. Ross Golden for his aid in interpretation of the films and assistance in the preparation of this paper.

### REFERENCES

- 1. Banyai, A. E. Direct and indirect pneumoperitoneum incidental to artificial pneumothorax.

  Am. J. M. Sc., 1933, 186, 513-518.
- BERGEMANE, W. Spannungspneumabdomen oder Gasperitonitis? Beitr. z. klin. Chir., 1932, 155, 597—203.
- BETTS, A. Subhepatic pneumoperitoneum demonstrated in gall-bladder films. Radiology, 1932, 18, 28-819.
- 4. Burch, L. E. Pneumoperitoneum as an aid in diagnosis of obscure pelvic lesions and early pregnancy. Surg., Gynec. & Obst., 1925, 40, 703-706.
- 5. Case, J. T' Review of three years' work and articles on pneumoperitoneum. Am. J. Roent-genol. 1421, 8, 714-721.
- CARELLI, F. H. Pneumoperitoneum. Am. J. ROENTGEWOL. & RAD. THERAPY, 1923, 10, 259-279.
- 7. Chiray, M., and Lomon, A. Pneumatose kystique de l'intestin et pneumopéritoine spontané. Prese méd., 1936, 44, 1771-1775.
- 8. COOMBS, H. C. Mechanism of regulation of intra-abdominal pressure. Am. J. Physiol., 1922, 62, 189-170.
- 9. COPHER, G. H. Demonstration of spontaneous pneum operationeum by roentgen ray; an aid in diagnosis of acute perforating peptic ulcer. J. Am M. Ass., 1924, 82, 781-783.
- 10. Dandy, W. E. Pneumoperitoneum. Ann. Surg.,

- II. Dehn, O., and Pčelina, K. Zur Frage über das spontane Pneumoperitoneum. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1937, 55, 187-191.
- 12. DELAFIELD, F., and PRUDDEN, T. M. A Text-Book of Pathology. Sixteenth edition. William Wood & Co., New York.
- 13. DE MONTMOLLIN, E. Le gaz du pneumo-péritoine. Rev. méd. de la Suisse Rom., 1930, 50, 116-118.
- ELRICK, L. Accidental pneumoperitoneum as a complication of artificial pneumothorax. Am. Rev. Tuberc., 1929, 19, 427-433.
- FORFOTA, E. Die Pneumatosis cystoides intestini im Röntgenbilde. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1936, 53, 131–139.
- FRIEDMAN, L. J. Clinical significance of pneumoperitoneum. Radiology, 1934, 23, 290-293.
- 17. Fritz, O. Auch ein Pneumoperitoneum. Wien. klin. Wehnschr., 1929, 42, 541-542.
- FÜHNER, H. Die peritoneale Resorptionszeit von Gasen. Deutsche med. Wehrschr., 1921, 47, 1393.
- FÜLLSACK, H. Spontanpneumoperitoneum bei Typhus abdominalis. Röntzenpraxis, 1930, 2, 330-332.
- GOETZE, O. Pneumoperitoneale Röntgendiagnostik. Deutsche med. Wehnschr., 1919, 45, 491-493.
- 21. HENKE, F., and LUBARSCH, O. Handbook of Pathology and Histology. Vol. IV, pp. 405-409.
- 22. Jacobaeus, H. C. Ueber die Möglichkeit die Zystoskopie bei Untersuchung seröser Höhlungen anzuwenden. München. med. Wehnschr., 1910, 57, 2090–2092.
- Johnson, S. E. Frequency of air under the diaphragm in perforated gastric and duodenal ulcer; report of 42 consecutive cases. J. Am. M. Ass., 1937, 108, 295–296.
- 24. Kelling, G. Ueber Oesophagoskopie, Gastroskopie und Kölioskopie. München. med. Wehnschr., 1902, 49, 21–24.
- Wehnschr., 1902, 49, 21-24.
  25. Kelloge, W. A. Spontaneous pneumoperitoneum demonstrated by x-ray in acute gastrointestinal perforations. New York M. J., 1921, 114, 294.
- KOPELOWITZ, M. Zur Kenntnis der Pneumatosis cystoides intestinorum hominis. Virchow's Arch. f. path. Anat., 1924, 248, 369-396.
- 27. LAURELL, H. Freies Gas in der Bauchhöhle. Acta radiol., 1925, 4, 590-602.
- LeWald, L. T. An experimental study of duration of artificial pneumo-peritoneum. Am. J. Roentgenol., 1920, 7, 502-504.
- 29. MacCharles, M. R. Spontaneous pneumoperitoneum. Canad. M. Ass. J., 1925, 15, 943-945.

- 30. Malcolm, J. D. Pneumoperitoneum of three days' duration following resection of carcinomatous rectum. *Lancet*, 1915, 1, 64-66.
- 31. Moberg, G. Two cases of pneumoperitoneum without any signs of perforation of alimentary canal or abdominal wall. *Acta radiol.*, 1937, 18, 798-806.
- 32. Monod, P., and Hollander, Contribution à l'étude du pneumopéritoine spontané. Bull. et mém. Soc. nat. de chir., 1932, 58, 940-947.
- 33. Overholt, R. H. Intraperitoneal pressure. Arch. Surg., 1931, 22, 691-703.
- 34. Peterson, R. Value of pneumoperitoneal roentgenography in obstetrics and gynecology. J. Am. M. Ass., 1922, 78, 397-400.
- 35. Salkin, D. Intraabdominal pressure and its regulation. Am. Rev. Tuberc., 1934, 30, 436-457.
- 36. Schindler, R., and Renshaw, J. F. Experimental study with certain tips used on Wolf-Schindler flexible gastroscope. Am. J. Digest. Dis. & Nutrition, 1936, 3, 747-751.
- 37. Schnitzler, J. Zur Kenntnis des Gasperitoneum. Wien. med. Wchnschr., 1929, 79, 987-989.
- 38. SINGER, H. A. Valvular penumoperitoneum. J. Am. M. Ass., 1932, 99, 2177-2180.
- 39. STENSTRÖM, B. Reflexionen über die Aetiologie des spontanen Pneumoperitoneums gelegentlich eines Röntgenbefundes. Acta radiol., 1937, 18, 625-634.
- 40. STEWART, W. H., and STEIN, A. Roentgen ray study of abdominal organs following oxygen inflation of peritoneal cavity. Ann. Surg., 1919, 70, 95; Am. J. Roentgenol., 1919, 6, 533-542.
- 41. URBAN, H. Anatomische und röntgenologische Befunde bei der Pneumatosis cystoides intestini. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1937, 55, 231-241.
- 42. Uspensky, A. E. Diagnostic importance of pneumoperitoneum. *Brit. J. Radiol.*, 1927, 32, 141–142.
- 43. WAGONER, G. W. Studies in intra-abdominal pressure; negative intra-abdominal pressure as normal condition. *Am. J. M. Sc.*, 1926, 171, 697–707.
- WARFIELD, C. H. Spontaneous pneumoperitoneum in ruptured peptic ulcer. *Radiology*, 1930, 14, 591–593.
- 45. Weber, E. Ueber die Bedeutung der Einführung von Sauerstoff resp. Luft in die Bauchhöhle für die experimentelle und diagnostische Röntgenologie. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1913, 20, 453-455.

# CARCINOMA OF THE JEJUNUM

# CASE REPORT

By J. H. HARRIS, M.D., and J. E. GREEN, M.D. CARLISLE, PENNSYLVANIA

THE following case is reported because of the rarity of preoperative diagnosis of carcinoma of the jejunum and because it illustrates the great importance of a careful study of the upper small intestine when vague abdominal complaints are presented.

The patient, male, single, aged twenty-seven, was referred for a gastrointestinal study in January, 1935. His symptoms consisted of discomfort in the upper abdomen with occasional vomiting. There was no pain and the history did not suggest any pathological entity. The routine roentgen study was negative.

Two years later, in January, 1937, the mark was referred for a study of the colon. His symptoms had persisted and he had developed a marked anemia. A mass was palpable in the left upper quadrant. The roentgen examination. of the colon was negative. On February 2, an enlarged cervical gland just above the left clavicle was removed for biopsy. The report by Dr. George Moffitt was metastatic adenocarcinoma. On February 18, an intravenous urogram showed the kidneys to be normal. The gastrointestinal tract was re-examined on February 20 and gastric peristalsis was found to be sluggish. The motility was markedly delayed, as none of the opaque mixture passed out of the stomach in thirty minutes. At the end of an hour enough barium had left she stomach to visualize the small intestine as far as the duodenojejunal junction. The duodenum was markedly dilated. At the end of three hours the barium had progressed a short distance along the jejunum and there was noted an area about 3 inches long in which all the feathery jejunal markings were obliterated and the bowel was a smooth narrow tube (Fig. 1). The roentgen diagnosis was neoplasm of the jejunum which had caused a severe grade of obstruction.

As the patient was losing weight and strength rapidly, it was felt advisable to explore the abdomen and perform a gastroenterostomy if possible. For this reason he was referred to the University Hospital, Philadelphia, where

Dr. E. L. Eliason performed an abdominal section on Masch 5, 1937 and reported the following: "I port opening the abdomen a mass about the size of a large orange was found in the meso of the first part of the jejunum. At a distance of 8 to 10 inches from the ligament of Treitz, there was a napkin ring constriction

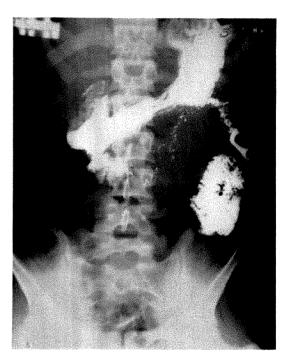


Fig. 1

of the portion of the jejunum passing over the domes of this mass. The entire section of the jejunum of which the mesentery was involved by the mass was hypertrophied and edematous, due in part to construction and probably in part to interference with blood and lymph drainage. A short circuiting anastomosis around the point of observation was done by bringing a loop of jejunum distal to the mass around its lateral side to the proximal loop just beyond the ligament of Treitz."The obstructive symptoms were relieved by this operation. The patient died of inaminon on September 4, 1937.

In reviewing the films of the first exami-

nation made in 1935, it was noted that a roentgenogram showing the upper small intestine was not made. At the six hour study the barium had passed the diseased portion of the bowel and hence it was overlooked. Although an hourly study of the small intestine of every case is advisable, this procedure is not feasible in many

roentgen offices and departments. However, every case should have at least one film made at such an interval as to show the entire small intestinal tract. Those patients having vague complaints, in whose routine study no disease is found, should certainly have a more careful small intestinal study.



# SACCULAR ABDOMINAL AGRTIC ANEURYSM\*

# AN ANALYSIS OF FORTY-EIGHT CASES

By M. J. HUBENY, M.D., F.A.C.R., F.A.C.P., 2007 SIMON POLLACK, M.D. CHICAGO, ILLINOIS

THE relative frequency of cases of proved saccular abdominal aneury m in the last few years at the Cook County Hospital prompted us to study the incidence, clinical picture, and roentgenological manifestations of this interesting and variegated clinical entity.

Investigation of the hospital admissions and postmortem records revealed that since 1926 there were only 48 cases of saccular abdominal aneurysm in which the diagnosis could be considered as established beyond reasonable doubt. Twenty-eight cases, or 60 per cent, of the total were confirmed by postmortem examination; 2 of these entered in shock, died within a few minutes of admission and were diagnosed by coroner's autopsy; 3 additional cases were confirmed by surgical exploration. The remainder were selected only where the diagnosis was well established by the clinical and roentgenologic findings. We have included only the saccular types, as the dissecting aneurysms do not characteristically show diagnostic roentgen findings.

## HISTORICAL

Although aneurysms as a clinical entity have long been known, the incidence of abdominal aneurysms has always been much less than those in the thoracic portions of the aorta. Ever since the first description of aneurysm of the internal vessels by Ambroïse Paré, the correlation between this condition and syphilis has been surmised. Even though Lancisi, William Hunter, and Morgagni in their classical studies of the gross anatomical features of internal aneurysm suspected a syphilitic etiology, and although they described the features of syphilitic aortitis, it was not till atter Schaudinn and Hoffmann discovered the Spirochaeta pallida in 1905 that the edologic importance of syphilis in aneurysm formation was proved by the demonstration of sprochetes in the involved aortic wall.

Kampmeer, in 1936, collected the cases of abdominal aneurysm from the records of the Charity Hospital of New Orleans for the past dirty years, and reviewed the literature of that date. His series included 68 cases. Thirty-eight of these were confirmed by autopsy; the others were well substantiated by clinical and roentgenologic findings. In reviewing the previous literature be referred to various collected series based both on autopsy and clinical materials, adding his 68 new cases to 313 previous y reported.

Since 1935, Neely reported 5 cases in a series of 1,25 postmortem examinations at Lincoln, Nebraska.

Mills and Horton, in reviewing all the cases of a neurysm at the Mayo Clinic in the years 1935–1936 included 80 cases of abdominal aneurysm. Besides these two series, reports of 22 isolated cases were collected from the literature from the period of 1938 to 1939.

## **ETIOLOGICAL FACTORS**

The age of the patients varied remarkably. As a rule, however, the incidence was greatest in the fourth and fifth decades. The unce lying pathological change producing the weakening of the aortic wall was without doubt the determining factor for the age period of greatest incidence.

Although the general hospital admissions are only about 40 per cent colored, the incidence nour series of 71 per cent is significant and can be interpreted as a consequence of the relatively high incidence of syphilis in the colored population of this region. The increased frequency in males

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as compared to females is an old observation. Kampmeier ascribed this difference to the fact that the activity of men entails more strenuous physical exertion, which places a greater tension on the weakened aortic wall. Likewise syphilis is more common in the male.

Of the underlying pathogenic processes, by far the most common were syphilis and arteriosclerosis. It is interesting to note the variable rôle that each of these played in the different series of cases studied. In our series and in Kampmeier's, where there was a high incidence of colored patients, syphilis was the underlying cause in the majority of the cases. Seventy-five per cent of our series showed evidence of syphilis either in the serology, history, or anatomical findings. Neely, on the other hand, in reporting his 5 cases collected from a series of autopsies in Lincoln, Nebraska, could not demonstrate evidence of syphilis in any instance. All his cases were white and in the older age group, comprised of the sixth to eighth decades. Mills and Horton, in their series reported from the Mayo Clinic, found that only 8.8 per cent of the 60 cases of abdominal aneurysm showed evidence of syphilis. Only one of their patients was a negro and he had syphilis; the age of over 86 per cent of their cases was above fifty-one years. In these latter groups of cases arteriosclerosis was the predominant pathogenic factor and hence the relatively higher age group involved. Our series of white patients included 9 of 14 over sixty-two years of age and 7 of these 9 had postmortem examinations which showed evidence of arteriosclerosis and none of syphilis.

Among the rarer causative factors are mycotic emboli involving the walls of the arteries. These are usually found in the vessels of moderate caliber such as the splenic and mesenteric arteries; none of our cases were of this type. Trauma also may play a rôle as Case I will illustrate. This patient had no evidence of syphilis or arteriosclerosis; the blood Wassermann and Kahn reactions were persistently negative. There

was a large pulsating mass in the left side of the epigastrium with audible bruit which was located at the site of the scar of an old abdominal stab wound incurred in a fight twelve years previously. Periarteritis nodosa may involve the moderate-sized abdominal arteries with resultant aneurysm formation. Wolff reports one such case showing multiple intra-abdominal aneurysms in the arteries of medium caliber. Infection from without may also involve the aortic wall and lead to aneurysm formation as illustrated by 2 cases reported by Dafoe where tuberculous aortitis and aneurysm

TABLE I

	ored	Col- ored Female	White Male	White Fe- male
Number of cases	26	8	12	2
Average age	45	40.4	66	38
Positive Wasser- mann or Kahn test	15 of 1	8 6	2 of 8 tested	I
History or anatomi- cal evidence of				
syphilis	22	7	5	0
Arteriosclerosis	0	0	7	1
Medionecrosis cystica	ı 0	0	0	1
Traumatic	1	0	0	0
Undetermined	2	0	0	0

developed secondary to adjacent caseous tuberculous mesenteric lymphadenitis. Medionecrosis cystica, a cystic degeneration of the elastic media with disruption of the elastic fibers of the aorta, is a rarer involvement and is usually associated with severe hypertension in younger individuals showing no arteriosclerosis. These processes are unusual and rare, and the only important pathogenic bases for aneurysm formation in the abdominal aorta are syphilis and arteriosclerosis. The relative importance of each of these depends on the race and age group of the patient. Syphilis is more common in the colored race and in patients up to the sixth decade; arteriosclerosis shows prevalence in white persons of the older age groups.

# SYMPTOMATOLOGY

The predominant complaint in almost all these cases was pain. The usual character-

istic of this pain was progressive increase in its severity with the progress of the disease; it usually occurred in the left side of the epigastrium as the greatest number of aneurysms were found in the upper thind of the abdominal aorta. As a rule, it radiated to the back in the region of the upper Lumbar spine and had associated shooting radiation to the left buttock, thigh, or even the whole left extremity simulating a sciatic neuritis. The pain was often described as boring or pounding and could often be relieved, at least temporarily, by changing from a supine to a prone position. As a rale, there was no relation to the intake of food, but one patient had the typical cyclacal pain of a duodenal ulcer syndrome.

Because of involvement of adjacent viscera, either by pressure or by compromising the blood supply, various symptoms of disturbance of the functions of these produced organs were present. Oftentimes these symptoms and findings obscured the presence of an aneurysm as the underlying causative factor. James reported a case of uremic coma due to compression of both renal arteries by a large abdominal aneurysm with secondary chronic interstitual nephritis. Case II in our series showed simulation of a primary kidney tumor by an aneurysm.

Gastrointestinal symptoms were often complained of as the stomach, duodenum, and colon are usually adjacent to the anewrysmal mass. Anorexia and associated weight loss were common complaints and may be a consequence of the pain. The presence of abdominal pain is in itself a finding associated most usually with inflammatory or ulcerative lesions in the upper gastrointestinal or biliary tracts. Washburn and Wilbur reported an interesting case from the Mayo Clinic which presented the clinical picture of a duodenal ulcer with pyloric obstruction and exploratory laparotomy revealed the stasis to be due to compression of the duodenum by an aneu-

Perforation of these aneurysms was usually posteriorly into the retroperitoneal tis-

sues and resulted in sudden onset of excruciating pain. This is due to the hematoma disserting up the fascial planes and disrupting the muscle fibers. Intra-abdominal, intra-horacic and intra-intestinal perforation is less common. The clinical picture of severe abdominal and lumbar pain, with associated shock and silent rigid abdomen, so simulate an acute surgical abdomen that the only 2 cases of our series who were examined in this extreme condition were both diagnosed as having perforated peptic ulcers.

The presence of other pathologic conditions may cloud the picture. Hutton and Galbraith reported a case in a taboparetic. This ratient developed a paraplegia and the destructive lesion of the lumbar spine with accompanying hypertrophic changes was considered for a time to be a Charcot's spine. Case III, reported below, showed abdominal aneurysm as an incidental finding in an ederly white male, whose death was correctly attributed to a recent coronary thrombosis.

The obysical findings when present were usually more reliable in arriving at a diagnosis. Of these, the presence of an expansilely pulsating abdominal mass was, as a rule, diagnostic. In a small group of the cases, the patient himself felt the mass before coming to the hospital. The expansile nature of the pulsation is peculiar and characteristic in that the palpating fingers are spread apart with each beat. This must be determined with utmost care, to rule out

TABLE II

SYMPTOMS AND FINDINGS IN FORTY-FIVE CASES

Sign	Incidence			
Palpable mass	33 cases, or 71%			
Expansile pulsation	30 of 32 cases with palpable			
• -	mass			
Bruit	17 of 20 cases where it was			
	looked for			
Thrill	8 of 15 cases where it was			
	looked for			
Pain	37 cases			
a. Radiation to back	29 cases			
b. Radiation to left				
lower extremit;	7 cases			

the usual type of abdominal tumors which transmit the aortic pulsation. A bruit can usually be heard over the mass and is due to the change in caliber of the vascular tube. Of the 20 cases of our series where bruit was looked for, it was present in 17. The palpation of a thrill over the mass was a more variable finding as the aneurysm wall may be thick and laminated. This finding was elicited in 8 of 15 cases where it was looked for. In those patients who showed erosion of the spine, marked localized tenderness was present over the dorsolumbar region; Murphy punch percussion over the left kidney area also showed marked tenderness in these cases. Differences in the pulsation and blood pressures in the lower extremities may contribute to the diagnosis. The findings of residual syphilitic lesions such as penile scars, syphilitic skin lesions or atrophic scarring, Argyle-Robertson pupils, perforation of the masal septum, or absence of the deep reflexes may help in arriving at a diagnosis of the syphilitic etiology of the process.

# ROENTGENOLOGIC FINDINGS

The characteristic roentgenologic findings, when present, are diagnostic and are resultant of secondary pressure defects on adjacent structures. The methods applicable in roentgen diagnosis of abdominal aneurysm include: (1) studies of the spine for erosion; (2) flat plates of the abdomen; (3) gastrointestinal studies; (4) pyelography; (5) pneumoperitoneum; (6) aortography.

By far the most common finding was erosion of the anterior portions of the vertebral bodies. Aneurysmal erosion is peculiar in that the intervertebral discs are spared giving a "scalloped" appearance to the erosion. Presumably the fibrocartilage being more resilient as compared to the vertebral bone resists the constant pressure of the aneurysm. When the descending thoracic or upper abdominal levels are involved the ribs may show erosion at their costovertebral angles. This is well demonstrated in Cases II and IV. In 10 of 23 of our series

where the spine studies were carried out, diagnostic erosions were present.

Although the flat plate of the abdomen may show nothing diagnostic, there may be important findings present. A soft tissue mass may be present, possibly delineated by intestinal gas shadows; if calcification can be noted in the region of the mass (usually seen in its walls) the finding is diagnostic for aneurysm. Erosion of the spine may, if extensive enough, show up in the flat plate of the abdomen. If the mass is large enough, the iliopsoas outline is obliterated and the kidney soft tissue shadow displaced simulating the findings noted in cases of retroperitoneal tumor. Five of 8 cases in which flat plates of the abdomen were taken showed diagnostic calcifications.

The presence and localization of intraabdominal tumors in general can often be accomplished by careful gastrointestinal studies. The roentgenoscopic examination is of most importance because not only was the mass oriented in reference to the adjacent gastrointestinal structures, but the presence of expansile pulsation could be directly observed. Pylography does not have this advantage and showed, as a rule, only extrinsic pressure displacement of the kidney (usually on the left side). Thirteen of 21 cases showed extrinsic pressure defects on the gastrointestinal or pyelographic studies.

Neither pneumoperitoneum nor aortography with thorotrast was carried out on any of these patients. Both procedures are not without certain risks which do not seem to counterbalance their possible diagnostic value.

## CASE REPORTS

The following cases are reported in some detail because of the interesting clinical and pathological findings:

Case I. J. W., a colored male, aged sixtyfive, entered the Cook County Hospital June 24, 1937. He complained of persistent pain in the abdomen to the left of the umbilicus. Ever since he was stabbed in the abdomen twelve years previously, for which emergency operation was performed, he had suffered vague pains in the abdomen at the site of the scar. In the past year these pains had become more severe and constant. About that time he noted this pain radiated to the left lumbar region. In the past ten days the radiation extended with increasing severity to the left buttock and thigh. No relationship was noted between the pain and intake of food except for slight aggravation of the "misery" with large meals. The patient denied any previous venereal infection.

On physical examination the temperature was 98.6° F., pulse 80, respiration 24, and biood pressure 130/80. Both pupils reacted to light and in accommodation. The heart and lurgs were essentially negative. An orange-sized mass was present in the abdomen to the left of the umbilicus with a definite expansile pulsation. The mass was not movable and no bruit as heard. The roentgenograms of the thoracolumbar spine revealed marked hypertrophic osteoarthritic changes but no evidence of erosun. The Wassermann and Kahn tests were negative on two occasions. The patient obtained some relief from analgesic medication and epideral injection and was discharged.

CASE II. R. S., a colored female, aged fortyeight, first entered the Cook County Hospital on March 18, 1936, with entrance diagnosis of abdominal tumor. Her chief complaint was a persistent pain in the left lumbar region with sharp shooting radiation of this pain down ker back to the left buttock. This had become progressively more severe for the past two months. Associated with the pain she had noted a mass in the left upper quadrant of her abdomen which had increased slightly in size during the past four weeks. No nocturia, frequency, hematuria or dysuria was noted. No other symptoms except progressive weakness and loss of an undetermined amount of weight were complained of.

She had had a normal menopause eight years reviously. About twenty years previously he was treated for "bad blood" by arm and hip "shots."

Physical examination at this time revealed a thin colored female suffering a good deal of pain. Temperature was 99.4° F., pulse 100, respiration 24 and blood pressure 110/70. The pulse were small and unequal and reacted sluggishly to light. A grapefruit-sized, movable mass was palpable in the left upper quadrant of the abdomen; no pulsation was noted at this

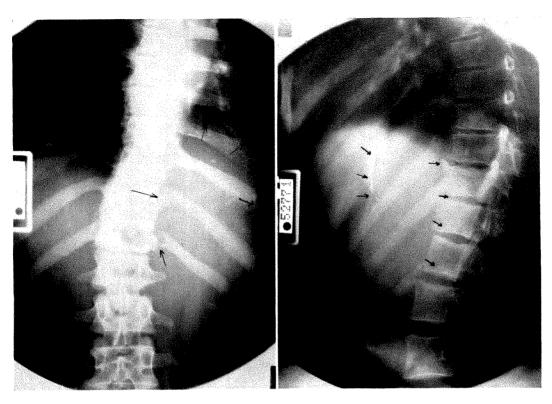
time. Vag mal examination revealed an atrophic uterus; no connection could be made out between the pelvic organs and the abdominal mass.

The fine gs were considered as due to a neoplasm in the left kidney. Roentgen studies of the stemach and colon revealed no evidence of extrinsic pathology. Hemoglobin was 65 per cent, sed 100d count 3,050,000, white blood count 5,700 Repeated urinalysis was negative for sugar and albumin, and no microscopic or chemical endence of urinary blood or pus was found. Repeated pyelograms showed a persistent filling defect of the upper calvces with narrowing and Sazziness of the calyces in the lower pole of the left kidney. The blood Wassermann and Kahn were both 4 plus. In spite of the absence of mematuria the genitourinary consultants considered the lesion as due to hypernephroma. After the nephrectomy incision was made and the pulsation of the mass noted, the lesion was parrectly diagnosed as aneurysm of the ablom nal aorta and further exploration deemed inacrisable.

The patient was discharged a few weeks later but due to he persistent severity of her pain had to be resomitted to the hospital on October 9, 1936 She had lost a good deal of weight and was much reaker than during her previous admission. He only relief from pain was obtained by maintaining a quiet position in bed on her left side with both legs flexed. At this time, although the sood pressure was equal in both arms, it was 40/100 in the right leg and 120/90 in the left. The heart was moderately enlarged and of zer ic configuration. A faint systolic murmu: 2011 be made out and that was apical. The aortic allness was between 6 and 7 cm. to percessies. The abdominal mass measured 10×12 cm. and had a definite expansile pulsation. A bruss was heard over it synchronous with the ratal pulse. The deep reflexes were normal and no pathological reflexes could be elicited.

The films of the lumbar spine at this time (Figs. 1 arz 2) revealed the characteristic erosion of the spine. The soft tissue shadow of the mass could also be made out with mottled calcification in its wall.

Because of the uncontrollable severe pain, a rhizotomy was considered for relief. On December 23, 1036, this was successfully done with resultant anesthesia on the left side to the level of 38. Ten days later on January 2, 1937, the papent died suddenly.



Figs. 1 and 2. Case 11. The large soft tissue aneurysmal mass is easily demarcated in the left upper quadrant of the abdomen. Note the erosion of the left side of the 11th and 12th dorsal vertebral bodies and the medial portions of the left 11th and 12th ribs. Diffuse calcification is present over the area of the mass. The erosion of the vertebral bodies is best noted in the lateral view.

Postmortem examination revealed the following essential anatomical findings: Huge aneurysm of the upper abdominal aorta with deep erosion of the lower thoracic and upper lumbar vertebrae and perforation through the diaphragm into the left pleural cavity; left hemothorax with compression of the left lung; brown atrophy and anemia of the myocardium; focal syphilitic aortitis of ascendens, arch and upper abdominal aorta; recent chordotomy.

Case III. F. J., white male, aged sixty-five, entered the hospital in September 30, 1937, because of the presence of a mass in the midportion of his abdomen which had become increasingly larger in size during the previous seven weeks. In 1929 he had suffered from an illness characterized by weight loss and weakness. At that time he was examined at the Mayo Clinic and treated for hyperthyroidism. For the following six and one-half years he had been in good health. However, six to seven months preceding this hospital admission he had noticed the presence of vague abdominal

pain localized to the umbilicus and not related to intake of food. In the past seven weeks he had become progressively weaker and lost about 35 pounds.

On admission, the temperature was 98 °F., pulse 88, respirations 20, and blood pressure 130/80. The pupils were round and equal and reacted to light and in accommodation. There was a large, firm, grapefruit-sized immovable mass in the epigastrium just above the umbilicus. There was a definite, expansile pulsation to the mass and a bruit was heard over it. The deep reflexes were physiological and no pathological reflexes could be elicited. There was palpable calcification of the radial arteries.

Laboratory study showed the following findings. The hemoglobin (Sahli) was 7.2 per cent, red blood cells 2,280,000, white blood cells 6,250. The blood Wassermann was negative on three occasions. Roentgen examination of the gastrointestinal tract revealed an extrinsic mass located behind and below the stomach, and above the transverse colon (Figs. 3 and 4). Expansile pulsation was noted on roentgeno-

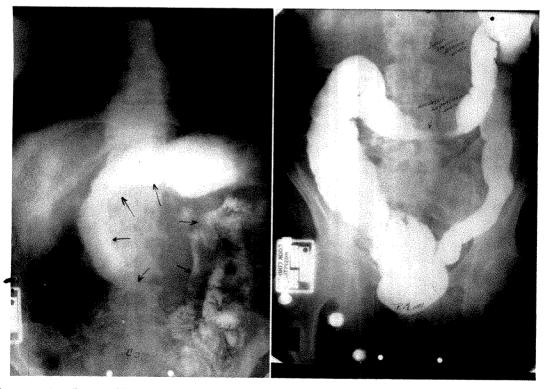
scopic examination. No erosion was noted in the lumbar spines. The electrocardiogram was interpreted as showing "auricular fibrillation with premature ventricular contractions. E-idence of severe myocardial damage. Left a is deviation. Inverted T2 and T3 seen in poster or coronary involvement."

The patient suffered from paroxysmal attacks of nocturnal dyspnea and died sudderly during one of the attacks, five weeks after admission. The clinical diagnosis was generalized arteriosclerosis with coronary sclerosis, myocardosis and arteriosclerotic abdominal aoric aneurysm.

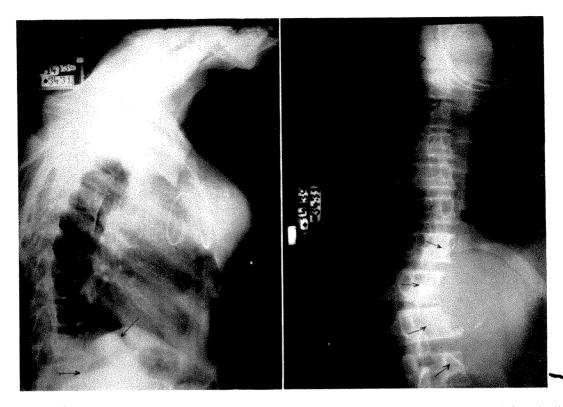
At postmortem examination the essential anatomical findings were as follows: Aneurysm of the abdominal aorta and right common iliac artery; severe atheroma of the abdominal aorta; severe sclerosis of both coronary arteries; postmyomalacic scarring of the posterior wall of the left ventricle and the interventricular septum; dilatation of both cardiac chambers; confluent bronchopneumonia of right lower pulmonary lobe; chronic cholecystitis and cholelithiasis.

CASE IV. R. A., colored male, aged fiftythree, was readmitted to the hospital on March 12, 1935, as an old case of thoracic aneurysm. He gave a listory of a chancre thirty-three years as; this was treated only by cauterization. He had no difficulty with the thoracic aneurysm for almost three years after it had been wired, but about three months before this admission he noted a definite enlargement and protested of the chest mass and recurrence of the old steady pain. About two weeks before entrance he developed severe steady pain in the back of his left knee and leg, and the leg collapsed when he tried to bear weight on it. He was unable to get about and, because of the severe on in both his chest and left lumbar region, Lad Leen unable to rest for the past two weeks.

On admission, the temperature was 98.6° F., pulse 80 and respirations 20. The blood pressure was 10.8/58 in the left arm and 98/60 in the right. The pupils were irregular in size and shape and fixed to light. There was a large protrucing mass about  $8 \times 9 \times 6$  cm. in the anterior porton of the chest in the region of



Figs. 3 and 4. Case III. The extrinsic defect pointes out by the arrows corresponds with the pulsating mass palpable and visible on roentgenoscopic examination. This is not as well demonstrated by the retrograde barium enema.



Figs. 5 and 6. Case iv. Note the marked erosion of the left side of the dorsolumbar spine. The left 12th rib is completely destroyed. Note the wired thoracic ameurysm which has eroded through the sternum.

the upper half of the manubrium. Definite expansile pulsation, bruit, and thrill were present over this mass. There was a similar large mass in the left side of the epigastrium about 15×12 cm. in size and the expansile pulsation could be felt through to the flank. There was marked tenderness in the left flank. There was also a similar mass, fusiform in shape, about 7×10 cm. in the left iliac fossa. The left leg was enlarged and edematous; no deep reflexes could be elicited and all sensation was absent in the posterior distal two-thirds and the anterior distal half of this leg.

The laboratory studies showed 4 plus blood Wassermann. Chest roentgenogram revealed a large mass arising from the aortic arch and protruding through the eroded manubrium sterni. Numerous loops of metal were seen within this mass. There was a similar round mass in the left upper quadrant of the abdomen. The bodies of the 12th thoracic and 1st lumbar vertebrae showed characteristic erosions; the left 12th rib was almost completely destroyed (Figs. 5 and 6).

The clinical diagnosis arrived at was recur-

rent syphilitic aneurysm of the thoracic aorta with erosion of the sternum; aneurysm of the upper abdominal aorta with erosion of the spine and compression of the left spinal nerves; aneurysm of the left iliac artery. The patient's condition in the hospital showed steady progression in size of the masses and in his weakness and weight loss.

# REFERENCES

- BISHOP, L. F., BISHOP, L. F., JR., and TRUBEK, M. Aneurysm of abdominal aorta. *Internat. Clin.*, 1935, ≥, 134-138.
- 2. ELLIOT, A. H., and EVANS, R. D. Clinical and electrocardiographic picture of coronary occlusion produced by ruptured aneurysm of the abdominal aorta. Am. J. M. Sc., 1936, 191, 196–200.
- 3. Dafoe, W. A., Ruptured aneurysms of abdominal aorta due to tuberculosis. *Edinburgh M. J.*, 1925, 32, 291–296.
- 4. Hartung, A. Diagnosis of abdominal aortic aneurysm. *Röntgenpraxis*, 1935, 7, 308–310.
- 5. Hutton, E. L., and Galbraith, A. J. Abdominal aortic aneurysm associated with general paralysis of the insane. *Lancet*, 1938, 1, 838–840.

- 6. James, T. G. I. Uraemia due to aneurysm of the abdominal aorta. Brit. J. Urol., 1935, 7, 157.
- 7. KAMPMEIER, R. H. Aneurysm of abdominal aorta; study of 73 cases. Am. J. M. Sc., 1936, 192, 97-109.
- 8. MILLS, J. H., and HORTON, B. T. Clinical aspects of aneurysm. *Arch. Int. Med.*, 1938, 62, 949-962.
- MINOR, J. Symptoms and diagnosis of ruptured aneurysm of the abdominal aorta. *Internex* Clin., 1938, 1, 144-153.
- Clin., 1938, 1, 144-153.
  10. NEELY, J. M. Ruptured abdominal aort≈
  Nebraska M. J., 1937, 22, 370-377.
- 11. OSLER, WILLIAM. Aneurysm of abdominal aorts. Lancet, 1905, 2, 1089.
- 12. Rusche, C. F., and Bacon, S. K. Ruptures abdominal aortic aneurysm simulating permephritic abscess. *Brit. J. Urol.*, 1935, 7, 33-332.

- 13. Spangen Beag, J. J., Munist, L., and Letjman, S. Aortografía. Aneurisma abdominal. Rev. Asoc. net argent., 1937, 50, 378-386.
- 14. Unger A. %, and Popper, M. H. Aneurysm of abdominal aorta. Am. J. Roentgenol. & Rad Therapy, 1936, 36, 523-524.
- 15. WASHFUEN R. N., and WILBUR, D. L. Obstruction of daodenum produced by aneurysm of abdom no aorta. Proc. Staff Meet., Mayo Clin., 1996, 11, 673-677.
- 16. WEINGROW, S. M., and BRAY, W. A. Aneurysm of a dominal aorta. Am. J. ROENTGENOL. & RAD. TF ERAPY, 1936, 36, 194-196.
- 17. WOLFE, K. W. Multiple aneurysms of abdominal aort. and large arteries with periarteritis nodesa. Virehow's Arch. f. path. Anat., 1936, 297, 177-206.



# NORMAL VARIATION IN THE GASTROINTESTINAL RESPONSE OF HEALTHY CHILDREN\*

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HERE is no single method completely satisfactory for determining the motility of the normal human's gastrointestinal tract, although this activity has fundamental significance in both health and disease. During growth, functional processes may be going on but there is no exact procedure for determining when the gastrointestinal pattern has become fully established; how much variation in motility exists among children within a narrow age range, when maintained under standardized conditions of environment, habit and food consumption; nor whether there exists any relation between motility and the absorption of various food components. The more recent studies in child development have made it evident that chronological age is of little value in estimating the degree of physiological maturity of an individual and that there are wide individual differences among children of a given

Growth is characterized by change. The healthy child may be considered as constituting "a universe in a state of continuous transformation";11 the rate of this transformation is governed by his individual physiological time and is therefore the result of heredity, previous environmental factors, and other forces. While the capacity for progress in physiological time is inherent in the individual, the degree to which a child attains his optimal rate is restricted by the current factors affecting his body processes: composition and bulk of the diet; the amount of activity and physical environment; exposure to deterrent influences producing Illnesses or dysfunction; habit; and, the state of mental and emotional contentment.

As a guide in timing the feeding interval,

physicians<sup>10</sup> have used roentgen examinations to study individual variations in the gastric motility of infants and have obtained data upon the time required for complete emptying of the stomach or the rate at which the food is expelled. Some of the studies on infants have not been limited to the stomach but have been extended to include the emptying time of the segments of the intestine;<sup>2</sup> however, few studies have been carried out with healthy children.

Three methods of study have been used by this laboratory to obtain information upon the rate of passage of food residues through the gastrointestinal tracts of average, healthy children who were subjects of an intensive investigation of the chemistre cf human growth.\* Serial roentgenological examinations have been made of the progress of test meals of barium sulfate in various media through the sections of the tract, to obtain an evaluation of the resoonse produced by different kinds of milks,<sup>14</sup> different types of foods (fat, protein, carbohydrate),15 and the variation in type or speed of response at different times. The motility of the entire alimentary canal has been studied from the records of the e apsed time between ingestion and defecation of carmine markers given every fifth day for eight consecutive months to separate the fecal units for analyses, by means of which to determine the retentions of nine chemical elements. 9,19 The possible effect of carmine was studied roentgenographically.12 The third method of study utilized the times, wet weights, and dry weights of the daily defecations during 225 consecutive days in which the same children were given a known, adequate dietary while liv-

<sup>\*</sup> Data procured during longitudinal and cross-section studies of the growth and development of preadolescent children are to be published in monograph form.

<sup>\*</sup> From the Research Laboratory of the Children's Fund of Michigan in cooperation with the Department of Roentgenology, Harper Hospital, and the Methodist Children's Village, Detroit.

ing in a healthful environment where habits of sleep, play, work and elimination were regular, and the frequency of defecations during twenty-six days of observation one and one-half years later. These three simple methods have enabled a coördinated study to be made of the mechanics of the digestive tract in relation to other physiological factors.

By roentgenoscopic and roentgenographic observation of the serial order of events

time of its exposure to the various digestive and assorptive processes throughout the entire digestive tract. This information permits more accurate clinical interpretations of reentgen observations in diagnosis of dysfunction in the tracts of children. Furthermore, the data contribute pertinent information to a better understanding of the physiology of the individual child as growth proceeds and aid in the interpretation of allied data on the retention and ab-

Table I

PHYSICAL DATA AND EMPTYING TIMES OF STOMACHS AND JEJUNUMS OF SEVEN CHILDREN IN RESPONSE

TO TEST MEALS OF EARIUM IN WATER AND IN MILK

Sub- ject	Sex	Age	Skele- tal Age*	Recum- bent Length	Weight	Physical Type†	Total—174 Roent-	Gastric tying	Emp- g Time	1	tying e of anum
		in de la company	7 igc	Length			genegrams	Water Milk	Water	Milk	
		(mo.)	(mo.)	(cm.)	(kg.)	THE PROPERTY OF THE PROPERTY O	per child	(hr.)	(hr.)	(hr.)	(hr.)
D.P.	M	117	129	143.5	345	0.0226	24	1.0	3.0	1.3	3.5
W.P.	M	113	106	126.2	278	0.0240	2.5	2.0	3.0	2.5	4.0
<b>1</b> 1.H.	M	102	97	129.7	25.36	0.0230	27	2.0	¥ . 5	3.0	2.0
F.C.	M	96	101	128.0	26.79	0.0234	-4	1.8	۵.۵	2.3	3.0
R.S.	M	88	85	123.7	22.36	0.0228	123	2.8	2.5	3.0	3.0
B.M.	F	81	79	114.7	19.07	0.0234	27	2.5	4.5	3.0	4.5
J.H.	M	74	66	117.4	21.91	0.0238	24	1.3	3.0	1.5	3.5
Mean				200				1.9	3.1	2.4	3.4

<sup>\*</sup> Assessed from roentgenograms (see first footnote page 30%).
† Cube root of weight divided by recumbent length.

occurring in the same individual at frequent intervals following the ingestion of a single test meal into a food-empty stomach, data may be procured on the emptying time of the stomach as distinguished from the intestinal rate—the latter is quite different and far more complex to investigate than the former; on the activity of the large intestine in contrast to that of the small—the large bowel is an organ that holds back material instead of pushing it on and ejects solid material only once or twice daily while the small intestine empties liquid into the colon continuously; on the type of dispersion of a particular barium meal as well as the kind of activity it produces in the different parts of the alimentary canal; and, the amount of surface presented by the ingested material and the

sorption of chemical elements, accumulated by metabolic balance determinations. A knowledge of the underlying physiology of the organs directly involved in the transformation of food into assimilable form and the rejection and ejection of the unused residue is fundamental in the interpretation of observations made in the clinic or laboratory.

## EXPERIMENTAL

The children, who served as the subjects of all the roentgenological, chemical, physiological, and clinical studies which are being correlated to appraise, in some measure, the phenomena of growth, had been under observation for several years and were known to be representative of average, healthy children; their medical histories revealed no known abnormal hereditary influences or excessive illnesses; they approximated the standards of weight for

height<sup>2,10</sup> (Table 1); possessed no subjective clinical symptoms, and were within the normal limits in skeletal development\* and mentality.† The assessments of skeletal maturity afford a possible basis for estimating the discrepancies between the chronological and physiological ages of the subjects (Table 1).

The children were maintained in a "home unit" in the rural environment of the Methodist Children's Village where they lived as a family with their housemother and had ample opportunity for recreation with toys and playthings, indoors and out, attended school and Sunday school, and lived in a comfortable, serene, homelike atmosphere.7.19 Their dietary, physical routine, and environment, comparable with those of the average, well child in an adequate "home" situation, were kept as constant as possible throughout all the studies. The children were familiarized with the purpose and method of each procedure, which facilitated the stimulation of regular habits and the cooperation and interest of all the subjects, thus minimizing the possibility of emotional states of fear, embarrassment, or anger, affecting the results.<sup>20</sup>

Each serial roentgenological study was initiated in the morning, at least one week following any previous examination. The subjects were restrained from ingesting any food or liquid (other than the test meal) between the evening meal preceding and the emptying of the test meal from the stomach. Each of the 7 subjects of this study was permitted to observe the roentgenoscopic examinations (L.R.) of the other children ingesting the water-barium meal. Each test meal consisted of 2 ounces of barium sulfate thoroughly mixed with 4 ounces of water or milk. The children's interest and familiarity with the procedures made possible the exposure of the first film in each series within twelve minutes after ingestion of the test meal. Examinations were made each half hour or hour thereafter until the stomach was empty. Additional roentgenograms were procured at intervals of twenty-four, fortyeight, and sometimes seventy-two hours after ingestion of the meals (total exposures of the 7 children, 174). All of the exposures were made with the child in prone position, the tube 31 inches from the film. Exposure was  $\frac{1}{5}$  sec. at 92

kv (peak), 50 ma., with 0.5 mm. aluminum filter and Potter-Bucky diaphragm.

t has been shown by Rowe<sup>17,18</sup> and others<sup>7</sup> that a change in gastric emptying time and colonic spasm, hyperperistalsis and other irregularities in peristalsis may be due to sensitiveness of the intestinal tract to foods and for this reason, in addition to the simplicity of its preparation, it has seemed advisable to use allergen-free mixtures of barium sulfate in water in the routine examinations of patients. Because routine roentgen observations are custo marily made with the water-barium test meal a knowledge of the variation in response produced by other media is essential in evaluating gastrointestinal response to the everyday m\_xed food dietary. The prominence of milk in the diets of infants and children and the indications that some individuals are sensitive to it make a comparative study of its effect upon the gastrointestinal motility particularly pertinent (the results of comparative studies of the response produced by other foods will be published in a following paper). To determine the permanency of the individual's particular response. the milk-barium series was repeated eighteen months later.

#### RESULTS

The roentgenoscopic examinations with the water meal verified the fact that, in all the children, the lung fields were clear, the heart shadow normal, none of the subjects had any thymic enlargement, and shadows of the liver and spleen were normal. In each subject the size and contour of the esophagus, stomach, and duodenal bulb were within the normal range. The duodenal bulb filled immediately in all cases. In one subject (R.S.) the stomach was noted to be I-shaped and rather large for a child of his age (Fig. 1). Although the configuration of the organs was within normal limits for all subjects, variations in size, shape, and pesition could be seen. These observations &rroborate those of Wright<sup>22</sup> who found in a study of 250 children, six to fifteen years old, that the position, size and shape of the stomach varies widely at all ages, showing a greater variation as puberty is approached. His observations also indicate that the sink-drain type of stomach is more common in younger children and the sharp hook type in older ones.

<sup>\*</sup> Evaluation of the skeletal development of the children was made by the late T. Wingate Todd, M.D., and C. C. Francis, M.D. of Western Reserve University, Cleveland.

<sup>†</sup> Psychological examinations were made by the Children's Center, Child Guidance Division of the Children's Fund of

<sup>‡</sup> The milk used was pasteurized and contained 3.5 per cent fat.

The gastric and jejunal emptying times of all the children with the water-barium and milk-barium meals have been esti-· mated from the complete series of reproductions and are presented in Table 1, together with pertinent data upon the physical measurements of the children. The average emptying time of the nutritive milk meals from the stomachs (3.1 hours) was more than 50 per cent longer than that of the inert water meal (1.9 hours); from the iejunum (3.4 hours), approximately onethird longer than that for the water (2.4 hours). The broad range of normal gastrointestinal behavior is emphasized by R.S. whose milk meal emptied from the stomach in less time than the water. However, in this case the possibility of a gastrointestinal allergy to milk cannot be discarded.5,15,16 Although R.S. gave no apparent allergic manifestations in his previous medical history, his skeletal tissues showed irregularities in density and maturity characteristic of allergic patients,\* his eosinophile count was high (an average for three different counts was 8.7 per cent whereas the average for a group of 10 children was 4.0 with a range from 1.5 to 8.7) and his skin test to milk protein was rated as one

For each of the subjects the water meal required longer to empty from the jejunum (average 2.4 hours) than from the stomach (average 1.9 hours). The average emptying times of the milk meals from both stomach and jejunum (3.1 and 3.4 hours) are slightly longer, respectively, than for the water meals (1.9 and 2.4 hours). In general, the children responded characteristically to the two different types of meals: those whose stamachs emptied more rapidly with the water meal than with the milk mixture (D.P., W.P., F.C., B.M., J.H.) showed a similarly greater motility of the water meal in the jejunum; the 2 subjects (H.H., R.S.) who showed slightly greater motility of the stomach with the milk meal had as rapid motility of the jejunum with the milk as with the water meal. The variations

ind cated by the differences in the ranges of the subjects' response to water and milk, in bota stomach and jejunum, are not significant for water or milk in either stomach or jejunum but indicate a greater variation with both meals in the jejunum.

Lttle or no absorption occurs from the stomach, but the gastric digested food undergoes the most profound digestive changes in the small intestine and it is here that most of the products of digestion are absorbed Intestinal digestion begins in the duodento about 8 to 10 cm. from the pylorus where the secretions from the bile duct emory and combine their action with that of succus entericus, thus introducing rapid and powerful proteolytic, amylolytic and lipolytic enzymes whose activities proceed simultaneously. Digestion and absorption may continue in the large intestine, out, in addition, excretion into the colon navalso take place.

In considering the amount of enzymatic activity to which a meal is subjected in various pertions of the digestive canal, it is of interest to consider not only the rapidity and type of filling that takes place in the stomach and intestines but the absorptive processes as well. It would seem that although the length of time required for a specified meal to pass through the tract or a section of the tract will indicate a measure of its motility, which may be affected by various factors such as the size of the meal, its temperature and consistency, the same interval cannot be used in estimating the length of time the meal is exposed to the varous digestive processes. Whereas the stornach is filled almost immediately upon ingestion of the meal, the emptying occurs over a much longer period of time. Althouga some of the meal may proceed immediately through the stomach and enter the intestine with scarcely an opportunity of being exposed to pepsin and other gastric drestive secretions, the last part of the meal may be retained until gastric digestion is quite complete before entering the intestine

The intest ne receives the contents of the stomach much more slowly than the stom-

<sup>\*</sup> Evaluation of the skeletal development of the children was made by the late T. Wingate Todd, M.D., and C.C. Francis, M.D. of Western Reserve University, Cleveland.



Fig. 1

F1G. 2

ach received the original food. Each portion, as it is ejaculated from the stomach, becomes subject to intestinal action and is exposed for the entire time required to traverse that section. The time of exposure in any section of the intestines may best be represented by the interval between initial reception and emission of a portion of the test meal.

Reproductions of the roentgenograms of the 7 children with the water and milk meals at four time intervals are shown in Figures 1 and 2. The roentgenograms obtained during the second examination with the milk-barium meal are shown in the same illustrations to facilitate comparison, but have been discussed separately. The individual variations in the patterns of these average, healthy children, as well as the variations in response to water and milk as the barium media, are apparent.

In Figure 1 the rapid initiation of gastric emptying and the diffusion of the water meal into the jejunum is obvious for all the subjects except B.M. who exhibited some anxiety before taking the meal. There appears to be an intestinal as well as gastric response to the type of medium used for the barium, for the greater motility of the water meals in the stomach was accompanied by faster progress through the duodenum and jejunum. The meal consisting of water and barium excited very feeble gastric peristaltic movements, unassociated with any pylorospasm, the mixture passing quite readily through the pylorus, but not quite so completely filling the duodenal bulb as the milk meal. The water-barium meal made its egress from the stomach in a fairly orderly manner, even during the first twelve minutes following the ingestion of the meal (Fig. 1).

The small bowel pattern was quite similar in all the subjects receiving the water-barium meal (Fig. 1) with very little evidence of peristalsis, per se, though there seems to be a fairly rapid passage of the water-barium meal through the small intestine, and the rate of passage of this particular type of meal is fairly consistent throughout the observations of all the sub-

jects. This may be seen in the exposures after twelve, forty, and eighty minutes.

There was an initial delay in the passage of the milk meal through the pylorus into the duodenum. Twelve minutes after ingestion of the meal, only 3 subjects (D.P., H.H., I.H.) show any of the milk-barium mixtures to have entered the small intestine, and gastric peristalsis was more vigorous than was observed with the water-barium meal. There seems to be a little more tone in the stomach filled with the milk meal, in comparison with the more or less relaxed appearance of the stomach with the water-barium meal. No inhibition of the gastric peristalsis can be observed, merely a delay in the passage of the barium out of the stomach. The small intestinal loops show considerably more peristaltic activity and churning effect than was observed with the water-barium meal, and there was a considerably longer time required for the passage of the nutritive milk-barium meal through the entire small intestine. In some subjects this delay was particularly prominent in the ileal loops. Throughout the observations the milk-barium meal produced similar patterns in the small intestines of all subjects.

The twenty-four hour exposures (Fig. 2) show that 4 subjects retained a large part of both the test meals in their colon after that interval; I subject's (F.C.) colon was well outlined with the milk-barium meal after twenty-four hours. The exposures made after the forty-eight hour interval show that the meals continued through the tracts and were eliminated at a rate consistent with the indications in the twentyfour hour exposures. In the group there is no apparent relationship between the length of the gastric emptying time and the motility of the entire tract. It is evident from the series of roentgenograms that the twenty-four hour exposure provides a fairly good index of the progress through the small intestine; however, it must be remembered that the twenty-four hour film was taken twenty-four hours after ingestion of the meal and that the length of time the meal was exposed to intestinal action

by the end of the twenty-four hours is the difference between the gastric emptying time and that figure.

Observation of the different patterns lustrated by the various series of pictures clearly defines the similarity in pattern between the twenty-four and forty-eight hour exposures making it obvious that any compensation or adjustment to the emptaining time of the stomach must take place

and one-half years after the first serial studies, under the same conditions of examination. While this later series of examinations was not preceded by eight months under conditions of rigid dietary and environmental control, the standardization of the subjects extended over five weeks and was more complete than would be encountered in clinical practice. Roentgenograms procured at comparative time inter-

TABLE II

EMPTYING TIMES OF STOMACHS AND JEJUNEWS OF SEVEN CHILDREN IN RESPONSE TO TEST MEALS

OF BARIUM IN MILK AT A.F. INTERVAL OF EIGHBIED MONTHS

	Gastric Em	ptying Time		g Time of mam	Defecations Per Day  Examination		
Child	Exam	ination	Exam	inazion			
	First	Second	First	Second	First*	Secondi	
	(hr.)	(hr.)	(hr.)	(hr.)	(hr.)	(hr.)	
D.P.	3.0	3.5	3.5	40	1.4	1.1	
V.P.	3.0	4.0	3.0	3.0	1.7	1.3	
1.H.	1.5	4.0	2.0	3-5	1.7	1.2	
F.C.	4.0	2.5	3.0	3-5	1.5	1.3	
R.S.	2.5	4.0	3.0	3.0	2,5	• 2.2	
3.M.	4.5	4.0	4.5	3.5	т.я́	1.2	
I.H.	3.0	3.5	3.5	1.0	2.0	1.4	
Average	3.1	3.6	3.8	32	1.8	1.4	

<sup>\*</sup> Average during eight consecutive months of metabolic andy.

within the first twenty-four hours, and, therefore, largely in the small intestine where the major activities of digestion and absorption take place. The patterns of the children whose gastric emptying these were longest demonstrate a decided acceleration of passage of the meal through the small intestine, which might be an incication that more extensive digestive processes in the stomach lessen those which must be performed in the small intestine, thereby producing greater motility in this part of the tract.

Normal Variation in Gastrointestina Response. To determine the possible range of variation which might be considered normal under clinical conditions of examination, the same milk-barium meal was observed roentgenographically in the gastrointestinal tracts of the same children one

vals are given in Figures 1 and 2, with the two preceding series, and the estimations of gastric and jejunal emptying time are presented in Table 11.

Inspection of the figures in Table II demonstrate the great variations in response to the same sest meal after eighteen months. possibly due to less complete standardization of the subjects or to changes resulting from progression of growth, with their resultant effect upon physiological maturity. The average of the gastric emptying times was increased in the second study; the average of the jejunal emptying times was decreased. The average number of defecations per day was less for each of the children during the twenty-six days within which the milk series was repeated than during the eight months of controlled study immediately preceding the first serial ex-

<sup>†</sup> Average during the twenty-six day period within which the examinations with the milk meal were repeated.

amination of the milk-barium meal in the gastrointestinal tract. The general average was 1.4 defecations per day as contrasted with 1.8 during the first series.

In Figures 1 and 2 the deviations in response to the repeated milk-barium meal in comparison with the earlier examinations are clear. After twelve minutes only I subject (F.C.) showed any of the barium to have passed out of the stomach into the small intestine. The type of peristalsis shown is practically identical, though there is a delay in its initiation. A similar orderly egress of the second milk-barium meal after gastric emptying started and the same rather slow passage of the meal through the jejunal loops may be observed. Only at the sixty minute period of observation did the jejunal and ileal loops appear fairly well outlined with the milk-barium mixture. This delay in passage of the mixture through the jejunal loops is probably explained by the slower emptying of the stomach, though in some of the subjects there seems to be considerably more segmentation of the small intestinal pattern in the later studies.

Once the barium mixture had passed through the small intestine into the large bowel, the rate of passage through the large bowel in most cases appears practically identical with the former series, except in the case of R.S., who showed an unusually rapid movement of all the meals through the large bowel compared to the other subjects. The extreme contrasts between the results of the two series accentuate the wide range of normal variation in gastrointestinal response which may be expected in roentgenological examinations of the same child at different times.

### SUMMARY

Serial roentgenographic studies of the gastrointestinal response of seven children between the ages of 74 and 117 months to test meals composed of 2 ounces of barium sulfate in 4 ounces of water and in 4 ounces of milk, ingested at body temperature, produced evidence that the variation in re-

sponse of different individuals, though wide, was not as great as the variation produced by the different types of media used. The observations recorded contribute pertinent information to a better understanding of the physiology and metabolism of the individual child and permit the determination of the range within which the estimation of normality may be made. They also permit a more accurate clinical interpretation of roentgen observations in diagnosis of dysfunction in the alimentary tract.

The results have greater significance because the subjects had lived together for a considerable period of time in the same highly controlled but happy environment where the food was known to contain adequate quantities of minerals,16 vitamins B and D,6,8 and other essential food components, and regular habits of elimination were established and known; the roentgen studies were made at the same time and at the season of the year when the alimentary tract is considered to be most active:20 the children were experienced and trained for months in roentgenographic and metabolic technique thus enabling complete coöperation and reducing to a minimum emotional disturbances such as fear, anxiety and anger.

Milk stimulated considerably more tone and vigorous peristalsis with churning effect in the stomach and a prolonged emptying time. Furthermore, milk caused a delay in the passage of the barium through the intestinal loops, particularly in the ileal portions. There were great variations in response of the individual subjects to the milk-barium meal after an interval of eighteen months, perhaps due to physiological changes coincident with growth, or to shorter preparation, and therefore less complete standardization of the subjects.

From the 174 roentgenograms of the gastrointestinal tracts of this group of specially controlled children the mean gastric emptying time in response to the waterbarium meal was 1.9 hours (range from 1.0 to 2.5); for the milk-barium meal 3.1 hours

(range from 1.5 to 4.5). The usual emptying time of the stomach is considered to vary from three to six hours, depending upon the emotional state of the individual, character of food, and other factors. 4,5,21 In all cases except one the water-barium meal entered the jejunum during the first twelve minutes after its ingestion. The emptying time of the jejunum with the milk-barium meal was 3.4 hours in contrast to 2.4 hours with the water-barium meal. There were no consistent, significant differences in the emptying of the colon as shown in the roentgenograms made twenty-four, fortyeight and seventy-two hours after the ingestion of the meals, indicating that any compensation or adjustment to the emptying time of the stomach must take place in the small intestine within the first twentyfour hours.

#### REFERENCES

- OLSON, M. B., and MACY, I. G. Relationship of gastrointestinal motility of growing children to fecal formation and excretion of food elements. To be published.
- 2. Bouslog, J. S., Cunningham, T. D., Hanner, J. P., Walton, J. B., and Waltz, H. D. Roentgenologic studies of infant's gastro-intestinal tract. J. Pediat., 1935, 6, 234-248.
- 3. BOYNTON, B. The Physical Growth of Girls. A Study of the Rhythm of Physical Growth from Anthropometric Measurements on Girls between Birth and Eighteen Years. University of Iowa Studies. Studies in Child Welfare, No. 4, 1936, 12.
- Cannon, W. B. Bodily Changes in Pain, Hunger, Fear and Rage. Second edition. D. Appleton Co., New York, 1929.
- Carlson, A. J., and Johnson, V. The Macainery of the Body. University of Chicago Press, 1937.
- Editorial. Vitamin B and gastric motility J. Am. M. Ass., 1926, 87, 852.
- FRIES, J. H., and ZIZMOR, J. Roentgen studies of children with alimentary disturbances due to food allergy. Am. J. Dis. Child., 1937, 54, 1239–1251.
- HARRIS, R. S., and BUNKER, J. W. M. Roentgenographic study of gastrointestinal motility in rachitic rats. Am. J. ROENTGENOL. & FAD. THERAPY, 1935, 33, 25-30.

- 9. Hummel, F. C., Hunscher, H. A., and Macy, I. G. Influence of fluid irradiated and evapora eccirtudiated milks on storage of nitrogen and action base minerals in children. Am. J. Dis. Chil. (in press).
- LADD, W. Influence of variations in diet on gastric modity in infants. Tr. Am. Pediat. Soc., 1943, 25, 74.
- 11. Du Neūv, F. L. Biological Time. Macmillan Co., N∗w York, 1937.
- 12. MACE, I G., REYNOLDS, L., and SOUDERS, H. J. Effect of carmine upon gastrointestinal motil ty of children. Am. J. Physiol., 1939, 126, 75-31
- 13. MERETTER, H. V. The Rhythm of Physical Goowth. A Study of Eighteen Anthropometric Measurements on Iowa City Males Ranging in Age between Birth and Eighteen Years. University of Iowa Studies. Studies in Child Wee face, No. 3, 1935, 11.
- 14. REYNDLES, L., MACY, I. G., and SOUDERS, H. J.
  Gestreintestinal response of children to test
  meals of barium and pasteurized, evaporated,
  and base-exchanged milks. J. Pediat., 1939,
  15. 1-12.
- 15. ReyNCLDS, L., MACY, I. G., and SOUDERS, H. J.

  The sestrointestinal response of average, healthy children to test meals of barium in milk, cream, meat and carbohydrate media.

  A.A. J. ROENTGENOL. & RAD. THERAPY (in press).
- 16. ROBERTSON, E. C. Intestinal stasis due to low materal intake. Am. J. Dis. Child., 1937, 53,
- 17. Rove, A. H. Food Allergy, Its Manifestations, Dagrasis and Treatment with a General Discussion of Bronchial Asthma. Lea & Febiger, Pallade phia, 1931.
- 18. Row E. A. H. Roentgen studies of patients with gastros intestinal food allergy. J. Am. M. Ass., 1627, 199, 394-400.
- 19. SOUDERS, H. J., HUNSCHER, H. A., HUMMEL, F. C. and MACY, I. G. Influence of fluid and of evaporated milk on mineral and nitrogen metabolism of growing children. Am. J. Dis. Cald. 1939, 58, 529-539.
- Told, T. W. Behavior Patterns of the Alimentary Fract. Williams & Wilkins Co., Baltimore, 1930.
- 21. Where House Conference. Growth and Development of the Child. Part II. Anatomy and Physiology, 1933, p. 629.
- 22. Wre HT; C. B. Gastric secretion, gastrointestinal meetility and position of the stomach. Arch. I st. I fed., 1924, 33, 435.

# THE LEAGUE OF NATIONS' WORK ON A UNIFORM. PRESENTATION OF THE RESULTS OF RADIATION THERAPY IN UTERINE CANCER\*

By J. HEYMAN, M.D. STOCKHOLM, SWEDEN

AS A continuation of its previous work on a uniform presentation of the results of radiation therapy in uterine cancer. the Health Committee of the League of Nations in 1935 decided to issue annual reports on the above results. The preparation for the issue of the annual reports was entrusted to an Advisory Committee the members of which are Lieutenant Colonel A. B. Smallman of the Ministry of Health, London, Dr. A. Lacassagne, l'Institut du Radium de l'Université de Paris, and myself. Dr. Mackenzie of the League of Nations Secretariat was appointed as secretary, replaced in July, 1936, by Dr. Wasserberg.

The primary object of the proposed annual statistical reports is to provide a convenient work of reference for those who need to know what can be said statistically in regard to the results obtained by the application of radiotherapy to patients suffering from cancer of the uterus when the agreed rules for the setting-up of statistics have been observed.

The First Annual Report<sup>1</sup> has recently been published dealing with the results obtained in 1930 and previous years. Cancer of the cervix only has been considered.

The number of collaborators in the First report has been limited in the main to clinics and countries which were associated with the earlier work of the Radiological Sub-Commission, because the Committee has recognized that its first report must necessarily be of an experimental nature to serve as a guide to its future work.

Statements have been submitted by: Centre des tumeurs de l'Université de Bruxelles

(Contributed by professor I. Mardoch)

Liverpool Radium Institute, England (Contributed by Dr. P. Malpas) Marie Curie Hospital, London, England (Contributed by Dr. E. Hurdon) Radium Centre for Carcinoma of the Uterus. London County Council, England (Contributed by Sir Comyns Berkeley) Institut du Radium de l'Université de Paris, (Contributed by Dr. A. Lacassagne) Radiumhemmet, Stockholm, Sweden (Contributed by Dr. J. Heyman)

The number of collaborators will gradually be increased. The Committee hopes that directors of clinics and others who are interested in this subject will communicate with the chairman with a view to future participation.

The Committee also hopes that the organized international collaboration in providing statements for the annual reports will lead to a clearer conception of the problems involved and will provide the experience which is necessary for their solution.

The Committee considers it to be one of its principal tasks to provide as far as possible for a uniform presentation of the data in order that the greatest possible comparability between statements from different clinics can be secured.

Mainly because of the unlike composition of the material at different clinics a certain lack of comparability is unavoidable. This fact makes it still more urgent to defeat any unnecessary deterioration of the comparability.

In order to facilitate a uniform presentation of data the Committee has adopted certain rules which collaborators are expected to observe. The rules are included in a series of tables and relevant notes. It is my intention to report on the tables and

<sup>1</sup> Series of League of Nations' Publications, C. H. 1225.

<sup>\*</sup> Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13-17, 1937.

the notes and to explain the guiding principles.

The first two paragraphs of the "Nones for Guidance of Collaborators" refer to the clinical type of cases which should be reported, namely cancer of the uterine cervix, including cancer of the stump. The Committee has considered it unsuitable to include for the present other types of utemovaginal carcinoma. Such a widening of the content of the statements must necessarily be preceded by a revision of the definitions of the different forms of uterovaginal carcinoma whereby it should particularly be considered how to differentiate between mdocervical carcinoma and cancer of the body and how to register cases where such a differentiation will not be possible.

Further the statement should be limited to cases where the treatment planned was essentially radiological. The Committee has preferred not to include for instance cases where a combined surgical and radiation treatment was originally planned until sufficient experience from less complicated circumstances will be available. Those tew cases which have been operated upon after failure of radiation treatment should not be counted as cured even if symptom tree after operation.

Thus the following clinical types should be excluded:

- 1. Cancer of the corpus uteri and vag a;
- 2. Recurrences after radical operation:
- 3. Patients primarily submitted to combined operative and radiation steatment.

Cases treated previously by radiat on elsewhere should also not be entered.

The third paragraph of the Notes states that "only those series of cases in which all clinical diagnoses have been microscopically confirmed can, as a rule, be accepted." The editor of the Report is empowered to invite the collaboration of institutes and individuals throughout the world but also to refuse statements which are considered not to be suitable. Paragraph 3 wants to emphasize that such statements only well be

considered suitable where microscopical diagnosis is not lacking in any considerable number of cases.

Only cases microscopically diagnosed as cancer should be reported.

Not only chorio-epithelioma, sarcoma and mal grant mixed tumors should be excluded but also precancerous conditions. The comparability of the statistics might be affected if the precancerous conditions were included which for the time being are very differently interpreted by the pathologists.

Paragraphs 5 and 6 stipulate:

- 5. The statement should relate to the total number of patients whose radiological treatment was begun during the year to which the statement refers as well as all patients examined with a view to treatment but not treated.
- 6. The statement should not be completed until a period of observation of at least five years from the beginning of the treatment has expired nal cases included.

These two paragraphs will be considered in the following.

Collaborators are requested to present their chirical material and the result of treatment in tabular form. On Table 1 should be stated:

- 1. The total number of patients examined with a view to treatment.
- II. Of those (1) the cases not treated and (2) those radiologically treated.

It is impossible to estimate the value of statistics if the material has been incompletely reported. The results derived from such statistics cannot be reliably compared with others. With a view to comparability all cases should therefore be reported.

Patients examined at the clinic but not treated should be specified in Table II. Patients referred to the clinic by means of letter, releptone, etc., which do not allow of their being examined at the clinic are excluded. In my opinion, such cases should also be reported if we want to avoid as far as possible any unfavorable influence on the comparability of the statistics caused by voluntary selection.

The total number of cases treated should be given in Table III grouped according to stages. The number of cases in which the microscopical diagnosis is lacking should be specified for each of the four stages. Lack of microscopical diagnosis is less significant in the advanced than in the early cases. In cases cured for five years it is considered to be sufficiently significant to justify the demand for a detailed description of each individual case.

The result of treatment should be stated in Table IV estimated after a period of observation of five years. The beginning of the five year period should coincide with the beginning of the treatment which is the only period that can be satisfactorily fixed. In the first column should be entered all cases treated, in column 2 those considered as cured at the end of the five year period, in column 3 patients alive but with recurrence, in column 4 patients alive operated upon after failure of radiotherapy, in column 5 those who have died from cancer of the uterus or as a result of treatment, in column 6 patients not traced and finally in column 7 patients dead from intercurrent disease, including those having died from cancer not primarily originating from the uterus.

A presentation of data according to the above recommendations is easily accomplished provided a suitable and effective organization is available. It seems to be a reasonable demand that different clinics should observe these recommendations when publishing their results.

The last three tables have reference to the calculation of the result.

A special chapter has been devoted to the discussion of the sources of error in statistical assessment of the result of treatment. The essential ones are due to smallness of the samples for analysis and to the lack of comparability between the clinical material. I will not enter upon the procedure adopted by the Committee in order to meet the difficulties related to smallness of the samples.

The main purpose in stating therapeutic

results is to allow a comparison of the results obtained at different clinics in order to estimate the value of the different methods of treatment used. Comparability is thus an essential condition which can, as mentioned above, be secured only to a certain extent.

The reason for this is that different radiotherapeutic clinics receive for treatment clinical material of unlike composition inas nuch as it contains different proportions of early or of late cases. Broadly speaking, the cause of these differences lies in the fact that, for some clinics, the material is not selected, for others a varying degree of intentional or unintentional selection takes place.

Some clinics, particularly in countries where hospital treatment is provided by the State, are responsible for the treatment of almost every patient from a defined area. There is practically no selection, the only patients not treated being those found unsuitable for treatment owing to the extent of the disease, general condition, etc. This involves nothing more than small differences which can be easily allowed for, provided all patients are included in the analysis whether treated or not.

Clinics of this type may be assumed to have non-selected and consequently comparable material. Such clinics may appropriately state the result of treatment by using the absolute cure rate, i.e., the ratio of the number of patients alive without recurrence to the total number examined, stated as a percentage. The absolute cure rate in one clinic is comparable with that of other clinics similarly circumstanced, but not with that of clinics in which selection necessarily takes place. The Committee has therefore suggested that clinics of the first mentioned type only should state the absolute cure rate.

In other clinics, a varying degree of selection may occur owing to such factors as inacecuacy of facilities for treatment or of bed accommodation for all patients who present themselves, or preference of the physician who first examines the patient

for operative or radiation treatment to then depending upon the degree to which radiotherapy has developed), and probably others. In clinics of this type, the composition of the clinical material may differ considerably and the results calculated from the total number of patients would be comparable only in exceptional instances. A comparison between such clinics is justifiable only when selection similar in kind and degree takes place. To estimate that similarity in selection would, however, be difficult and is hardly possible unless detailed knowledge of the organization of the different clinics in this respect is available.

When such knowledge is available an over-all relative cure rate (calculated on the total number of patients treated) may have a certain value. It is clear, however, that over-all relative cure rates should be compared only exceptionally and with discrimination.

In order, so far as possible, to meet the difficulty of non-comparability between clinics dealing with selected material, the dividing of the cases into different groups according to the spread of the growth has been resorted to. The samples included at different clinics in one and the same stage should provide uniform material suitable for comparison. It should, however, be noticed that by "staging" the effect of selection on the comparability becomes reduced but not eliminated. Each stage contains a series of more or less advanced cases which

will make a selection not only possible but—part cularly in clinics with small facilities—to some extent unavoidable.

Further it should be emphasized that in staging nothing but the anatomo-clinical extent of the growth is considered whereas other factors which may affect the prognosis, and thus vitiate comparability, are entirely neglected. In this connection may be mentioned severe infection, serious disease of other organs, senescence, pregnancy and other complications which may prevent completion of treatment or ultimately cause the death of the patient before the five year period has expired. Such instances will uncombitedly occur more frequently in clinics dealing with selected material.

Another disadvantage accompanying this device for assessing comparability is that the arbitrary rules adopted for allotting cases to the various stages are interpreted by different clinicians in a different way thereby defeating still more the effect to assess the comparability of the samples. Consequently a certain lack of comparability is attached to the cure rates for different stages.

In order to reduce further the last mentioned cisadvantage the Committee has proposed to supply the verbal definitions of the four stages with illustrative diagrams. The Health Organization of the League of Nations has decided to issue such an Atlas, which will probably appear in print within six months.





# THE TREATMENT OF INFECTED HEMANGIOMATA\*

By ERNST A. POHLE, M. D., Ph.D., F.A.C.R.
Professor of Radiology, University of Wisconsin Medical School
MADISON, WISCONSIN

R ADIATION therapy has become established as the method of choice in the treatment of vascular nevi. Although there are some radiologists on the continent and perhaps a few in the United States who are using roentgen rays, radium is considered in this country to be the most valuable agent in the treatment of angiomata at present. Depending on the type of lesion we have to deal with, surface applications (plaques, screens) or interstitial radium (radon seeds, platinum filtered radium needles) are chosen and, if properly used, give good cosmetic results in approximately 75 per cent of the cases treated. This does not include the so-called nevus flammeus (port wine mark) which is not suitable for radiation therapy.

One complication which occurs occasionally in hemangioma is trauma followed by ulceration and secondary infection. A search of the literature did not reveal many references to this subject. MacKee<sup>5</sup> in the latest edition of his book on "X-Rays and Radium in the Treatment of Diseases of the Skin" mentions it only casually, and Andren,1 who analyzed and reported the cases of nevi seen at the Radiumhemmet in Stockholm from 1909 to 1924 states: "If the hemangionsa happens to be traumatically ulcerated when admitted, it is nowadays given immediate radiological treatment, for it has been found that the ulcerated surface clears up quickly with such treatment at the same time as the hemangioma becomes reduced in size."

In order to obtain further information on this subject questionnaires were mailed to a group of 30 well known radiologists and dermatologists throughout the country. We received 14 replies, 12 of which could be used in this survey. The following questions were asked:

- 1. How many cases of infected vascular nevi have you seen?
- 2. What is the approximate percentage of incidence in your own cases?
- 3. Do you recommend radium therapy of infected vascular nevi?
- 4. If the answer to Question No. 3 is in the affirmative, please state if you vary the dose as compared with noninfected vascular nevi.

The answers are compiled in Table 1. The majority of observers and especially those who see a large number of cases report a very small percentage of incidence of ulcerated hemangioma varying from 0 to 5 per cent. Only one physician estimated it at 10 per cent and another at 25 per cent. The majority advise radium treatment in the infected hemangioma and there is a definite tendency to use smaller doses than in the noninfected type. Several radiologists recommend the treatment of the infection by roentgen rays, followed by radium applications.

We believe the incidence of infection to be fairly low because in 152 patients with bemangiomata observed during the last cecade at the Wisconsin General Hospital only 4 cases with infections were seen; 3 were angiomata and 1 was an angiofibroma. Therefore, it seemed worth while to us to report our experience in their treatment.

#### CASE REPORTS

Case I (X-ray No. 3843). A female child aged five months, was referred to the Depart ment of Radiology on April II, 1934, for treatment of an ulcerated vascular nevus on the inner aspect of the left thigh at the junction of the ower and middle thirds (Fig. I). This nevus was present at birth. About a month before admission the skin in the center broke down and an ulcer developed. The entire nevus grew rather rapidly and in spite of local treatment

<sup>\*</sup> From the Department of Radiology and Physical Therapy, State of Wisconsin General Hospital, Madison, Wisconsin. Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.

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TABLE I

Answer	Question 1	Question 2	Question 3	Question 4
I	0	0	Ž es	V <sub>O</sub>
2	5	2.5%	િંહ	Depends on size of lesion and extent of infection
3	4	2.8%	Y ::3	Smaller dose
4	25	25%	Y	Surface application until ulcer is healed, then interstitial radium
5	0	0	Yes	<b>1</b> 50
6	4 or 5	Under 1%	Yes	Smaller dose
7	2	5%	After infection	
8	i	10 $C_{C}$	Y =s	No
9	Many	10%	Ræntgen rays	Smaller dose
10	12	Under 1%	N:	Uncertain
11	12	۶	Ă e s	Smaller dose
12	2 or 3	Under 1%	I C	Roentgen rays firs, then smaller dose of radium

there was no tendency to heal. The lesion was divided in two areas and a 2×2 cm. radium plaque containing 10 mg. radium element fletered through 0.1 mm. Al was applied to 90 m areas for a period of one hour. The lesion responded well to the treatment. On May 3 a second application was given with the sure technique but this time for only forty minutes. Re-examination at monthly intervals showed complete healing of the ulcer and disappearan respectatic areas at the edge. The child was seem last on February 24, 1939, approximately five years after the first visit; the cosmetic end-result is satisfactory (Fig. 2).



Fig. 1. Case 1. Ulcerated angioma on left thigh in April, 1934.

Case is (X-ray No. 5404) A female child, aged three months, was referred to the Department of Radiology on March 10,1936, for treatment of at ulcerated vascular nevus involving part of the flexor and extensor surfaces of almost the entime left arm (Fig. 3). This lesion was present at birth and there was marked interference with motion. The family physician had treated it by means of ointments and several exposites to the quartz mercury vapor lamp. Because of the size of the lesion it was divided into several areas which were treated by means of heavily filtered radon screens



Fig. 2. Case 1. Appearance of scar in February, 1939.



Fig. 2. Case 11. Ulcerated extensive angioma of left arm in March, 1936.

(equivalent to 2.0 mm. brass). Six screens were applied on March 10, 1936, at 3 cm. distance for a total dosage of 300 mc-hr. Another area was treated on September 15, 1936, with the same technique and dose, and a therd area on October 14, 1936, requiring only four screens. The ulcer healed within three months after the first application and by February, 1937, most of the hemangioma had disappeared; there was full range of motion at the elbow. Residual angiomatous tissue on the dorsal left forearm was treated with seven radon screens (same technique as above) but at 1 cm. distance for a total dosage of 100 mc-hr. Re-examination in February, 1939, showed no evidence of angioma, but a soft pliable scar throughout the treated areas without interference with motion (Fig. 4).

Case III (X-ray No. 4605). A male child, aged two and a half, was admitted on July 17, 1934, to the Wisconsin Orthopedic Hospital for Children. He had a large tumor in the region of the right thumb, which according to the parents had been present since birth (Fig. 5A). The growth measured 7 inches in circumference at the base of the thumb. There was a fluctuating erythematous swelling surrounding it and over this area there was increased local heat. Roentgen examination showed soft tissue swelling but no involvement of the bone. The fluctuating area was incised and pus was obtained. The cul-

tures showed a *Streptococcus haemolyticus*. Tissue was removed for biopsy; the histological diagnosis was angiofibroma (Fig. 5B). Hot dressings were applied and on the date of discharge, October 5, 1934, the circumference of the tumor had decreased by 2 inches.

The patient was readmitted on March 16, 1935. The tumor was smaller and softer and the biopsy wound had healed (Fig. 6A). Radium screens were applied at a distance (five screens filtered through 0.5 mm. silver plus 1.0 mm. brass, 3 cm. distance, total dose 300 mc-hr.). R2-examination on June 30, 1935, showed no decrease in the size of the tumor and after consultation with the Department of Orthopedics it was decided to attempt excision followed by further irradiation (Fig. 6B). The tumor was removed and the defect skin grafted on June 2, 1936. On August 5, 1936, eight radium screens were applied to the site of the former lesion for a total dose of 300 mc-hr. The patient

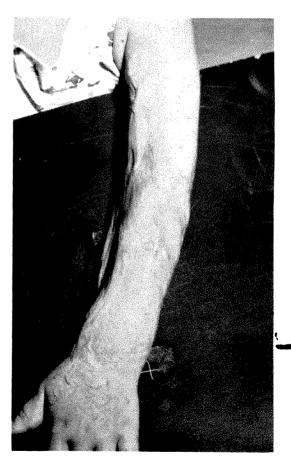


Fig. 4. Case II. February, 1939. End-result after treatment.

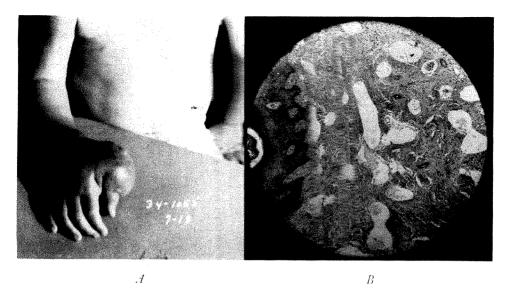


Fig. 5. Case III. A, angiofibroma on admission July 7, 1934; B, photomicrograph showing very fibrous growth with numerous blood vessels. The lumen of many of these is almost completely occluded by fibrous tissue and proliferated endothelium. (Published by permission of the Mississeppi Valley Medical Journal.)

was seen again on February 8, 1937. The skin graft was somewhat redundant and angiomatous tissue extended into the web between the thumb and finger. The patient did not return to the hospital until June, 1938, when a massive recurrent tumor mass was present (Fig. 7A. Five 1 mg. radium needles of 2.5 cm. length filtered through 0.5 mm. Pt were inserted into the lesion and left in place for five days to de-

liver a total desage of 600 mg-hr. The response was very gratifying and on September 30, 1938, two needles were inserted in the residual angiomatous tissue. They remained in place for seven days for a total dose of 336 mg-hr. When last seen in April, 1939, the cosmetic result seemed to be satisfactory (Fig. 7B). There was no evidence of recurrence and motion of the thumb was good.

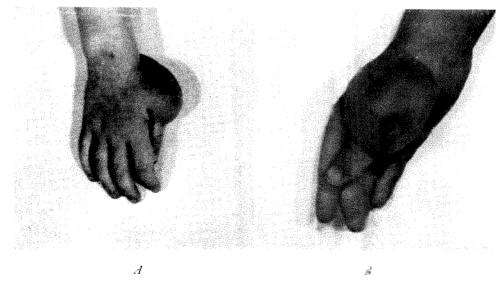


Fig. 6. Case III. A, appearance of growth on March 16, 1935. The biopsy wound has healed. B, appearance of growth on June 30, 1935, after first application of radium screens. (Published by permission of the Mississippi Valley Medical Journal.)

Case IV (X-ray No. 6944). A female child, aged eight weeks, was referred to the Department of Radiology on September 30, 1937, for treatment of an extensive angioma of the left forearm (Fig. 8). This lesion was present at birth and resembled then a sumburn; it grew thicker and deeper in color. In order to determine the radiosensitivity the 10 mg. radium plaque filtered through 0.1 mm. Al was applied to a selected area at a distance of 0.5 cm. for

gicma. The ulcers became infected and the parents decided to take the baby to another clinic for additional consultation. She was immediately hospitalized and the infected areas were treated by local applications of potassium permanganate (1-10,000) one or two times daily for two weeks, then replaced by Macey's ointment (composed of haliver oil 10 parts, cod lizer oil 50 parts and 10 per cent zinc peroxide ir white petrolatum 100 parts) for eleven days



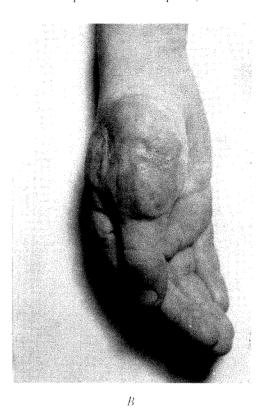


Fig. 7. Case III. A, recurrence on admission, June 14, 1938; B, appearance of lesion on January 24, 1939, after implantation of platinum radium needles in June and in September, 1938. (Published by permission of the Mississippi Valley Medical Journal.)

thirty minutes. When seen a month later the response had been most striking and therefore a second area was treated with the same technique. Three weeks after this application the skin broke down in both treated areas. A week later a mild hemorrhage occurred in one ulcerated area. Two weeks later further ulceration developed scattered throughout the untreated region so that this apparently had no connection with the radium treatment. The surgical consultant considered the possibility of a necplasm and a biopsy was done. However, the microscopic examination showed only a hemar-

and then returned to the application of potassium permanganate for eleven more days during which time the infected areas continued to improve. The child was dismissed on February 18, 1938, at which time the lesion had decreased to less than the size of a silver dollar. The mother was instructed to continue Macey's ointment and to bandage the lesion. She returned with the child August 11, 1938, stating that the wound had been completely healed for four months. She had no complaint and there was no apparent limitation of motion.\*

<sup>\*</sup> It was impossible to obtain a photographic record of the end-result.

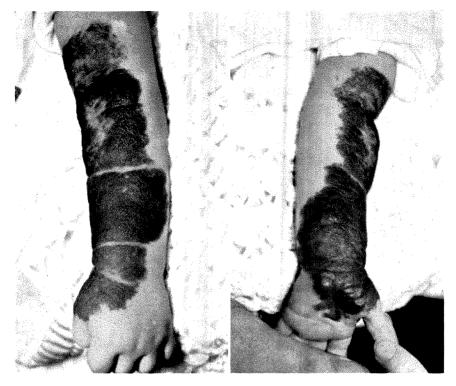


Fig. 8. Case iv. Extensive angioma on left arm in September, 1937.

#### COMMENT

There are a few general rules to be followed in the treatment of angiomata by radium. The superficial lesions can be taken care of successfully by means of a contact plaque containing 2.5 mg. radium element per square centimeter which is filtered through o.1 mm. Al. For deeper lessions, heavily filtered radium screens emisting only gamma rays and applied at distances of from 1 to 3 cm. are indicated. In either case erythema reactions should be avaided and the intervals between sittings must be sufficiently long to allow the effect of a previous treatment to subside complete. It seems advisable to treat infected amgiomata with smaller doses and increased intervals between exposures as compared with the noninfected type. In supericial lesions, the radium plaque may suffee as shown in our first case and satisfactory cosmetic results can be obtained. The carernous type of angioma requires gamma rays and apparently repeated exposures over a

long period. This is demonstrated in the second case which represented very extensive ulceration with involvement of parts of the flexor and extensor sides of almost the entire arm. There is no reason why roentgen mays should not be effective in treating the inflammation. Although we have no experience of our own in this respect, the procedure has been recommended by others (see Table 1).

A different approach had to be chosen in the third case. Histologically it belonged to the more radioresistant group of angiofibroma and here the ulceration followed incision of an abscess, whose etiology remained unknown. Radium surface applications were unsuccessful but implantation of radium platinum needles with low radium content brought about satisfactory regression of a massive recurrence which had ceveloped after excision, plastic repair and external radium therapy. This method of treatment is also valuable in large cavernous angiomata as well as in lesions

which are technically difficult to handle by means of surface applicators.<sup>2,3,4</sup> The fourth case is interesting in view of the observation reported in the literature that cavernous angiomata occasionally regress spontaneously following trauma, ulceration or fibrosis. While the initial response to radium therapy was striking, ulceration occurred not only in the two treated test areas but diffusely in the entire involved region. Ordinary antiphlogistic treatment resulted in almost complete disappearance of the lesion without additional radium therapy.

#### SUMMARY

- 1. Radium is recognized as an efficient single therapeutic agent in the treatment of angioma (vascular nevus and cavernous angioma).
- 2. Infection is not a contraindication to radium therapy. However, smaller doses than those customary in the noninfected type are advocated with increased intervals between treatments.
- 3. Four illustrative cases of infected hemangiomata are reported. Their incidence is apparently low because in a series of 152 consecutive cases seen during a decade it corresponded to approximately 2.6 per cent.

#### REFERENCES

- Andren, G. Radium treatment of haemangiomata, lymphangiomata and naevi pigmentosi. Experiences from "Radiumhemmet," 1909– 1924. Acta radiol., 1927, 8, 1-45.
- Ваемяен, W. Über die Radiumbehandlung der Hämangiome. Strahlentherapie, 1939, 63, 496– 505.
- 3. Brown, J. B., and Byars, L. T. Interstitial radiation treatment of hemangiomata. Am. J. Surg., 1938, 39, 452-457.
- 4. Edwards, H. G. F. Interstitial use of low radium content monel metal needles in treatment of angiomas. Am. J. Roentgenol. & Rad. Therapy, 1938, 40, 899-902.
- 5. MacKee, G. M. X-Rays and Radium in the Treatment of Diseases of the Skin. Third edition, Lea & Febiger, Philadelphia, 1938.
- 6. Ронье, Е. А. Radiation therapy of anglofibroma. Mississippi Valley M. J., 1939, 61, 41-43.

#### DISCUSSION

DR. J. R. DRIVER, Cleveland, Ohio. Infected hemangiomas are not common. As a rule one is likely to see these lesions in locations similar • to the ones Dr. Pohle described, for instance the inner surface of the thighs where the skin is liable to become infected by contamination with feces and urine, and I have seen these lesions a number of times on the vulva and in the intergluteal region.

Very often they are a mixed type, for example, a strawberry or capillary nevus on the surface, combined with a cavernous nevus in the base.

I agree with Dr. Pohle that irradiation helps these cases and that they heal more promptly. However, I think one should use care in the dose he employs. Smaller doses than those recommended in this paper, I believe, would be equally effective.

The healing of the infection itself has a tendency to have a beneficial effect on the hemangioma. We all know that many years ago it was the custom to vaccinate lesions of this kind in order to produce an infection, the healing of which worked out pretty well for small lesions. Naturally, it wasn't so good for the large lesions.

The treatment of hemangiomas requires individualization in many instances. It is not just a question of using radium, roentgen rays, or solid carbon dioxide. Combinations of various methods are often required.

Large capillary port wine nevi are radioresistant and respond poorly to any type of therapy. If seen within the first few weeks of life, one may use light treatments with the radium plaque or with roentgen rays. While the response may appear slight, or negligible, yet I believe such efforts may well prevent some of the late sequelae, such as the development of the deep port wine color, the late appearance of tumor-like growths, and possibly the alteration of growth of surrounding structures resulting in asymmetry.

The so-called nevus flammeus is yet another type of capillary nevus seen in the region of the center of the forehead, over the eyelids, dorsum of the nose, and nape of the neck. This type often disappears spontaneously. However, they sometimes persist. These lesions respond well to light radium treatments if given before the child is six months old.

The strawberry type of hemangioma is quite

radiosensitive if treated early. This was illustrated in the splendid result obtained by Dr. Pohle in his patient who was treated, I believe, at the age of eight weeks. Personally I would have used a smaller dose. If I understood him correctly, he used a filter of o.1 mm. of aluminum on a half strength plaque with exposures of thirty minutes. With contact treatment this would produce a severe reaction.

Cavernous hemangiomas are generally deeply seated and may grow rapidly. They are radiosensitive and should be treated as early in life as possible, if the best results are to be obtained. Irradiation can be given by means of reentgen rays or radium. Interstitial irradiation by means of gold emanation seeds I feel is unsatisfactory. Foreign body reactions about the seeds may necessitate surgical excision later. In those cavernous hemangiomas which do not respond to irradiation, I have obtained satisfactory results from the injection of sciencing solutions into the tumor.

DR. ZOE A. JOHNSTON, Pittsburgh, Pa. I have treated 6 cases of infected nevi. The locations were interesting. One involved the end of the nose in a young man; the rest were infants, one on the back in the sacral region, the other a little higher in the sacral region, and ] were around the vulva, and inner thigh regions.

I have had the same experience as the others have had. It is better to proceed with caution when planning the treatment. Sometimes a week or two of preliminary treatment, if there is very much infection, does help to lessen the reaction following irradiation.

DR. G. W. GRIER, Pittsburgh, Pa. 4 saw a baby once that had a cavernous angicma on the scalp, and while the mother was trying to make

up her mind whether she would have the baby treated or row, the nevus became infected, and following the healing of the infection the resultant scar politerated the hemangioma and it didn't need treatment. Personally, I am not sure that infection of angiomas is an unmixed evil.

DR. POHEE (closing). Regarding the dose that is used in the implantation of radium needles. The patient had in June, 1938, five 1 mg. macilim needles of 2.5 cm. length filtered through 0.5 mm. Pt, inserted in the lesion and left in place for five days to deliver a total dosage of 500 mg-hr. The response was very gratifying and on September 30, 1938, two needles were inserted in the residual angiomatous tissue. They remained in place for seven days, for a total dose of 336 mg-hr.

I was esseed about the disturbance of bone growth in the case where the screens are used at distance. We have never observed any, although I have no evidence in the form of roentgen saudies of the bones involved. But if we can be from growth only, there has been no untoward effect.

As regards the dosage to the child which showed wheration, I should have stated, as in the text, that the plaque was applied at a distance of mm. and at such distance we, at least, do not see any severe reactions in the skin.

Someone else asked me to mention the treatment of angiomata near the eye. We treat those, also, and if we do we make use of a set of various sized screens made of lead and plated with platinum. They are inserted over the eyeball and under the lid, and this provides complete protection. We do not get any reactions in the eyeball.



## ARTHRITIS AND PARA-ARTHRITIS TREATED WITH THE ROENTGEN RAY

#### REPORT OF 161 CASES

By TOBIAS B. WEINBERG, M.D. NEW YORK CITY

THE treatment of arthress, rethritis and neuritis by roentgen irradi-HE treatment of arthritis, para-aration has not received the recognition it deserves. The response of some painful joints to roentgen irradiation is frequently so dramatic that it surprises both the patient and the therapist. In recent years various forms of therapy have been tried in the treatment of arthritis as well as bursitis, neuritis and myositis. Some observers report good results with vaccine treatment; others claim cures with hyperpyrexia or radiotherm. Obviously it is difficult to evaluate the various forms of therapy because the diseases in question vary widely in their duration, their underlying causes and the pathological changes present. Therefore, very similar pathological or roentgenological changes may be associated with entirely different symptoms, Occasionally no evident symptomatology exists in spite of the advanced roentgenographic changes. For example, we frequently see spondylitic changes in the spine with associated lipping and bridging of the bodies of the vertebrae without pain, whereas similar roentgenographic findings in another case may give excruciating pains.

#### HISTORICAL

The treatment of arthritis with roentgen rays dates back to 1897 when Sokolow<sup>1</sup> first attempted it. In 1898 Stenbeck<sup>2</sup> reported 52 cases with 80 per cent improved. In this country Anders, Daland and Pfahler3 in 1906 reported a great improvement following the use of roentgen treatment. Langer4 reported good results. More recently de Lorimier<sup>5</sup> reported excellent results with roentgen therapy in para-arthri-

In 1931 I started treating arthritis and

other painful joint conditions with roentgen irradiation and first presented my results on December 12, 1933.\* Since beginning the use of this form of treatment, over 160 cases have come under my observation and care.

### FORMS OF PARA-ARTHRITIS TREATED

I shall not attempt to give a detailed history of all the cases treated but shall select a typical specimen of some of the major groups and give a short history of the case as well as the results of the treatment. In this series of cases were included arthritis, mainly of the hypertrophic variety; bursitis, the large majority of which were subdeltoid and subacromial; spondylitis involving the cervical, dorsal and lumbar Some were diagnosed neuritis, whereas others were just labelled algias such as metatarsalgia, neuralgia, etc. Still others were called rheumatism.

The cases treated according to anatomical location are as follows:

- 1. Shoulder (a) arthritis (b) bursitis
- 2. Cervical spine—spondylitis Dorsal spine—spondylitis Lumbar spine—spondylitis
- 3. Sacroiliac arthritis
- 4. Knees—arthritis (Hypersophic)
- 5. Feet—arthritis
- 6. Miscellaneous: (a) torticollis (b) metatarsalgia (c) herpes zoster (d) neuralgia following extraction of teeth.

#### SYMPTOMS

The predominant and often the only subjective symptom was pain of variable intensity and duration. The pain was frequently excruciating and the patient in-

<sup>\*</sup> Cases presented at the meeting of the East Side Clinical Society on December 12, 1933.

capacitated. Some of the associated symptoms were limitation of motion, tenderness, swelling, rarely temperature and malaise. A large percentage of these patients had positive roentgenological findings. The presence or absence of roentgenological evidence of disease, however, was not considered the criteria for instituting the treatment. Pain was always the primary indication for therapy.

#### HISTORY AND ETIOLOGY

The ages ranged from ten to seventyfive years; the youngest patient treamed was a boy aged ten and the oldest was a man aged seventy-five. The sexes were almost evenly distributed. The duration of symptoms varied from a few days to twelve years. The most acute cases suffered only a few days; the most chronic one had symptoms over a period of twelve years. Except for the complaint in question nearly all of the patients were otherwise in good physical condition. Occasionally trauma preceded the onset of pain. In 2 patients a neuralgia of the face followed the extration of a molar tooth. A subdeltoid bursits was caused by a fall on the shoulder in one patient and in another a severe pain in the lumbar region was brought about by a sudden twist of the back while attempting to prevent his falling downstairs. A large percentage of the cases were either physicians or their immediate family. This fact facilitated following up many of these patients. Most of the patients had tried various other forms of therapy before being referred for roentgen treatment. Quite a number had intramuscular or intravenous medication, others had nerve block and still others had had operations for the relief of the painful condition. Most of the operations were for the removal of supposed foci of infection and included tonsillectomy, appendectomy, oöphorectomy, nasal accessory sinus drainage, dental extraction, etc. Many had tried orthopedic appliances, plaster jackets, frames, shoes and various types of splints. Most of the patients had taken therapeutic baths.

#### DIAGNOSIS

The diagnosis of the cases referred for therapy varied. Some were easily diagnosed such as a acutely painful shoulder with a calcified deposit in the region of the bursa. Other cases were more difficult to diagnose and included painful joints with no physical signs and no roentgen findings. Many cases were incorrectly diagnosed, a dorsal spondy itis with radiculitis being frequently thought to be a coronary disease. Cervical sportdyliris with pain radiating to the shoulder and upper extremity was called arthritis of the shoulder by the physician referring the case. Some who had a lumbar spondylitis were diagnosed renal calculus and another was called metastasis. Roentgenography was helpful in clearing up the diagnosis in many cases.

#### PATHOLOGY

The most frequently demonstrable pathological finding was a deposit of calcium in the region of the affected joint. The deposit was either outside of the joint as seen in bursitis or visualized within the joint as in osteo-error ts. Occasionally erosion of the joint surfaces was noted.

#### TREATMENT

The treatment was given directly over the involved area. The dosage was 100 to 150 r two or three times weekly and varied from three to twelve treatments. The factors were 30 kv., 4 ma., 0.5 mm. Cu plus 1.0 mm. Al, 50 cm. focal skin distance and the fields varied from 10 by 10 cm. to 15 by 20 cm., depending upon the size and the position of the involved area.

In my experience the shorter the duration of the symptoms the sooner the condition was alleviated, and the more chronic cases required a longer period of time to bring about satisfactory results. In other words, the acute cases responded to fewer roentgen treatments than the more chronic. It is essential to warn the patient that there may be a reaction following the first few treatments, associated with aggravation of symptoms, occasionally malaise and



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						TABLE I				
Case	Name	Sex	Age	Occupation	Diagnosis	Part Affected	Duration	Treatment Began	No.	Result
I	W.N.	М	55	Physician	Bursitis	L. shoulder	Few months	12/28/31	I	С
2	LW.	M	42	Undertaker	Calcified bursitis	R. shoulcer	Few months	4/26/32	2	C
3	M.R.	M	5.5	Physician	Bursitis	R. shoulcer		8/ 2/32	2	C
4	M.K.	M	51	Cutter	Spondylitis	Lumbosæcroiliac spine	1 year	8/ 9/32	3	C
5	I.F.	M	42	Operator	Spondylitis	Lumbar spine		10/ 6/32	5	C
$\vec{6}$	J.R.	M	60	None	Spondylitis	Lumbar spine	6 weeks	1/ 5/33	2	C
7	L.M.	F	5.5	Housewife	Spondelitis	Sacroiliac	3 weeks	2/ 9/33	7	C
8	E.S.	M	10	School	Torticollis	Neck	i week	6/26/33	4	C
9	E.F.	F	42	Housewife	Spondylitis	Lumbar spine	1 year	10/ 7/33	3	C
10	L.N.	М	58	Butcher	Sacroiliae ar- thritis	Sacroiliae and knee	Few years	10/10/33	7	C and Rec
11	N.G.	M	30	Lawyer		L. hip	2-3 years	11/4/33	4	С
12	D.K.	F	51	Housewife	Spondylitis	Lumbosacroiliac spine		12/19/33	4	С
13	J.E.	M	47	Furrier	Calcified bursitis			3/ 7/34	3	C
14	R.S.	F	34	Housewife	Torticollis	Neck	Few weeks	3/14/34	3	Not imp
15	E.S.	M	10	School	Torticollis	Neck	Recurrence	3/17/34	5	C
16	R.D.	F	49	Housewife	Spondylitis	Lumbar spine	6 weeks	0. 7.01	~	C
17	E.O'C		49	Fireman	Calcified bursitis		Few months	4/ 4/34	2	C
18	J.G.	M	50	Garageman	Arthritis	Shoulders	ı year	4/18/34	Few courses	Imp
19	V.C.	F	27	Housewife	Bursitis	L. shoulder	10 days	4/21/34	2	C
20	J.W.	M	43	Furrier	Spondylitis	Dorsal spine	Few years	4/22/34	3	Imp
21	J.C.	F	40	Housewife	Neuralgia	Face	Few days	5/ 4/34	2	·C ·
22	L.M.	F	26	Office work	Spondylitis	Lumbar spine	Few months	5/ 9/34	I	Imp
		M			Bursitis	L. shoulder	3 weeks	$\frac{3}{9}, \frac{9}{34}$	3	C
23	J.M.	F	42	Physician	Calcified bursitis		1 week	$\frac{3/21/34}{5/28/34}$	3 4	Č
24	L.R.	- M	48	Housewife	Spondylitis	Lumbar spine	6 years	6/ 1/34	Course	č
25	K.F.		53	Housewife	* *	Lumbar spine	1 month	$\frac{6}{2/34}$	I	č
26	H.F.	M	31	Business	Spondylitis		5 weeks	$\frac{6}{5/34}$		č
27 28	M.G. G.S.	M F	36 42	Salesman Housewife	Spondylitis Spondylitis	Lumbar spine Cervico-dorso- lumbar spine	16 years	6/14/34	6	Imp
2.0	C.S.	M	20	Salesman	Spendylitis	turrour spine	3-4 days	6/23/34	í	C
29			0.7	Business	Arthritis	Feet	Few months	7/ 9/34		č
30	J.G.	M			Arthritis	Knees	2 months	$\frac{77.97.34}{7/14/34}$	• 3 3	Imp
31 32	F.S. J.W.	F M	63 60	Housewife Retired	Spondylitis, ar- thritis	Sacroiliac, knees		7/30/34	5	Imp
2.2	T.B.	М		Undertaker	Spondylitis	Lun bosacral	3 months	8/ 7/34	7	Imp
33	H.L.	M	~ *	Physician	Arthritis	Sacroiliac	10 years	8/15/34	3	Imp
34	A.L.	M	w w	Baker	Arthritis	L. shoulder	6 weeks	8/15/34	3	C
35 36	M.H.	M	- 1	Physician Physician	Arthritis Spondylitis	L. snoulder Cervical spine	Few weeks	8/17/34	1	lmp
37	LL.	M	44	Dentist	Arthritis	Sacroiliac	8 days	8/27/34	Course	C
- 37 - 38	P.D.	M		Plumber	Spondylitis	Lumbar spine	Few months	9/18/34	1	C
-	A.S.	M		Truckman	Spondylitis	Lumbosacral	3-4 weeks	9/23/34	2	Č
39	R.B.	M		P.O. clerk	Bursitis	R . shoulder	2 years	10/ 5/34	5	Ċ
40	A.L.	F		Housewife	Spondylitis	Lu nbosacral	6 months	10/ 6/34	7	Imp
41			50	Housewife	Spondylitis	Ce-vical spine	2 weeks	10/31/34		C—later
42	M.K. A.R.	F F	57 44	Housewife	Arthritis	Kr ees and sacro-		11/ 8/34		recurred Imp
43					Arthritis	liac R . shoulder	17 years	11/12/34		Imp
44	R.W.		40			L. shoulder	5 months	$\frac{11/12/34}{11/21/34}$		Imp
45 46	M.H. E.K.	F	A 10		Archritis Metatarsalgia	Pain in the rt.	-	11/21/34		C
47	J.N.	F	65	Housewife	Arthritis	L shoulder	1 week	12/ 4/34	3	С

C = Complete relief Rec = Recurrence Imp = Improved

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					Tabli	E I—Continued				
Case	Name	Sex	Age	Occupation	Diagnosis	Part Affected	Duration	Treatment Began	No.	Result
	c p	N 1		C	Company to Mark		TS	/ 0/a.		C
48 49	S.R. F.D.	M F	57 29	Cutter Housewife	Spondylitis Neuralgia	Lumbar spine Following tootl extraction	Few months Few days	12/8/34 $12/31/34$	5 2	c
50	A.C.	F	55	Housewife	Spondylitis	Dorsolumbar	ş ≪ears	1/ 2/35	Two courses	С
51	L.M.	M	50	Examiner	Spondylitis	Lumbar	Few years	1/20/35	I	Imp
52	S.L.	F	38	Saleslady	Spondylitis	Cervical spine	6 months	$\frac{2}{5}$	Two	C '
•			·	•	Arthritis	R. shoulder			courses	
53	N.G.	F	55	Physician	Arthritis	Shoulders	Few years	2/ 5/35	Three courses	Imp
54	L.R.	F	47	Nurse	Arthritis	R. shoulder	3 weeks	2/ 2/35	2	С
55	M.R.	$\mathbf{F}$	50	Editor	Osteo-arthritis	Shoulders	2 gears	2/12/35	4	Imp
56	M.A.	F	48	Secretary .	Neuralgia	Headaches	Few years	2/12/35	1	lmp—later sterilized
57	M.K.	F	43	Nurse	Spondylitis	Lumbar	15 years	2/25/35	6	Imp
58	C.T.	F	28	Stenographer	Spondylitis	Cervical	Fe∓ months	2/27/35	2	С
59	J.Z.	$\mathbf{F}$	51	Housewife	Spondylitis	Lumbar	2 months	3/ 8/35	7	C
60	R.C.	F	58	Housewife	Spondylitis	Cervicodorsal	25 years	3/18/35	I	Imp?
61	M.P.	$\mathbf{M}$	41	Tailor	Spondylitis	Cervical	24 years	4/ 2/35	3	C
62	G.I.	$\mathbf{F}$	65	Housewife	Spondylitis	Cervical	5 months	4/ 3/35	3	C
63	A.W.	$\mathbf{F}$	50	Secretary	Spondylitis	Cervicodorsal	4 sears	4/18/35	11	C
64	L.Z.	M	45	Insurance	Spondylitis	Cervical	26 darys	4/22/35	5	С
65	J.S.	M	55	Business	Arthritis Spondylitis	R. shoulder Cervical	5 months	4/27/35	12	С
66	M.D.	M	61	Mechanic	Spondylitis	Lumbosacral	4 weeks	5/ 2/35	11	C
67	R.G.	$\mathbf{F}$	45	Housewife	Arthritis	Hands	Few months	5/ 6/35	8	Imp
68	A.A.	$\mathbf{F}$	47	Housewife	Spondylitis	Cervicodorsal	26 years	5/14/35	8	Imp
69	M.M.	$\mathbf{F}$	64	Housewife	Arthritis	Sacroiliac	i vear	5/13/35	4	Imp
70	M.D.	M	41	Policeman	Spondylitis	Dorsal	4-3 years	5/13/35	4	C
71	S.S.	M	48	Salesman	Arthritis	R. shoulder	6 weeks	6/17/35	5	Imp
72	M.K.	F	39	Housewife	Calcified bursits	L. shoulder	8 davs	6/25/35	3	Imp
73	M.F.	$\mathbf{F}$	38	Housewife	Spondylitis	Cervical	2 weeks	6/26/35	4	C
74	G.F.	M	65	Retired	Spondylitis	Lumbosacroilize spine	months	7/ 6/35	7	Imp?
75	A.G.	M	38	Printer	Spondylitis	Dorsal spine	3 years	7/15/35	5	Imp
76	R.E.	F	75	None	Spondylitis	Lumbar	2 weeks	7/18/35	5	Imp
77	R.G.	F	44	Maid	Spondylitis	Sacroiliac	2 months	8/27/35	3	Imp
78	J.P.	M	44	Physician	Neuralgia	Headaches	Few years	9/ 3/35	3	Imp
79	B.F.	F	42	Housewife	Metatarsalgia	Right great to	Few months	9/11/35	4	C
80	L.T.	M	55	Physician	Spondvlitis	Cervicodorsal	Few weeks	9/17/35	2	Č
81	R.G.	F	30	Housewife	Arthritis	Left elbow	2情 vears	9/19/35	2	Imp
82	I.B.	M	27	Student	Arthritis	Sacroiliac	6 menths	9/23/35	6	Imp
83	J.R.	F	40	Housewife	Spondylitis	Cervical	I Wells	10/ 8/35	6	C T
84	T.W.	F	42	Housewife	Spondylitis Arthritis	Cervical Shoulders	Few months	10/ 8/35	15	Imp
85	F.F.	$\mathbf{F}$	50	Housewife	Arthritis	R. shoulder	i year	10/ 8/35	3	Imp
86	F.C.	F	50	Housewife	Spondylitis	Lumbar	1 Wear	10/14/35	I	Imp?
87	S.S.	M	35	Business	Spondylitis	Cervical	3. racenths	10/31/35	6	Imp
88	E.S	M	60	Business	Spondylitis Arthritis	Lumbar Sacroiliac	3. years	11/21/35	5	C
89	M.B.	$\cdot \mathbf{M}$	5.5	Physician	Arthritis	Elbows	Few months	11/ 2/35	2	Imp
90	S.K.	F	48	Housewife	Spondylitis	Cervical	i maonth	11/26/35	2	Imp
91	M.R.	$\hat{\mathbf{F}}$	35	Nurse	Spondylitis _	Lumbar	3-4 months	12/ 9/35	2	Imp?
92	J.M.	M	50	Dentist	Calcified bursitis		Few months	12/10/35	4	Imp
93	M.L.	M	55	Physician	Arthritis	L. shoulder	Few months	12/19/35	4	C T
94	T.Z.	F	55	Butcher	Spondylitis	Cervical	Few months	12/27/35	7	Č
95	E.S.	M	33 42	Physician	Spondylitis	Cervical	Few weeks	12/23/35	3	Imp
96	LG.	F	44	Housewife	Spondylitis	Cervical	Few months	1/28/36	$\ddot{6}$	C
	E.S.	M	32	Physician	Spondylitis	Cervical	Few weeks	2/ 1/36	4	č
-			., -		L					-
97		F	75	Housewife	Spondylitis	Cervical	Pew weeks	2/24/36	2	C
-	A.B. A.G.	F M	75 60	Housewife Physician	Spondylitis Shingles	Cervical Chest	Few weeks Few weeks	2/25/36 3/16/36	2 2	C C

TABLE I-Continued

Case	Name	Sex	Age	Occupation	. Diagnosis	Part Affected	Duration	Treatmen Began	t No.	Result
10	I.M.	F	35	Housewife	Spondylitis	Cervical	I vear	4/ 8/36		C
02	H.R.	M	40	Lawyer	Spondylitis	Cervical	Few months	4/ 0/30 4/26/36	5	Imp
03	S.G.	M	40	Physician	Spondylitis	Cervical	3-4 months	5/ 1/36	4	
04	J.A.	M	50	Physician	Herpes zoster	Chest and L.	Few months	6/16/36	2 6	C C
05	M.R.	M	40	Dentist	Spondylitis	shoulder Cervical	o waalso	07.07.7	_	C
06	A.B.	F	55	Housewife	Spendylitis		2 weeks	8/18/36	2	C
07	M.H.	F	35 35	Housewife	Arthritis	Lumbar	2 months	12/ 5/36	6	Imp
08	A.L.	F				R. sacroikac	ı year	12/19/36	П	Imp
	E.R.	F	5.5	Housewife	Arthritis	R. shoulder	Few months	12/20/36	6	lmp
09	J.F.	F	5.5	Housewife	Arthritis	All joints	Few years	1/ 6/37	21	Imp?
10	j.r.	r	48	Housewife	Arthritis	Shoulders	1 year	1/ 7/37	13	C
11	Y.G.	F	38	Housewife	Spøndylitis Arthritis	Cervical	r ı	, ,		
12	A.S.	M	55 55	Clerk		Sacroiliac	Few weeks	2/21/37	3	C
	S.G.	M			Arthritis	Right hip	Few weeks	2/13/37	12	C
13			55	Retired	Arthritis Spondylitis	L. shoulder Cervical	3 months	4/ 2/37	10	Imp?
1.4	B.K.	F	21	Housewife	Calcified bursitis	Subacromial	Few weeks	4/ 4/37	2	C
15	I.H.	M	32	Dentist	Calcified bursitis		Few weeks	4/24/37	4	č
16	R.M.	F	36	Housewife	Spondylitis	Cervicodorsal	i year	5/ 4/37	10	Č
17	J.B.	M	35	Mechanic	Arthritis	L. shoulder	1 year	5/ 6/37 5/ 6/37	10	Imp
18	R.S.	F	60	Housewife	Spondylitis	Lumbar	Few years	5/ 7/37		
19	S.K.	M	65	Retired	Amhritis	L. shoulder	* .		14	Imp
	J.R.	M	45	Garageman	Spondylitis	Lumbar	3 months	5/10/37	3	Imp
	W.G.	M	40	Salesman	Spondylitis		2 months	5/11/37	4	Ç,
	S.G.	M	50	Business	Spondylitis Spondylitis	Lumbosæral	Few months	5/11/37	6	Imp?
	L.G.	F		Housewife		Lumbar	ı year	5/28/37	15	Imp
24	A.G.	M	35	Porter	Arthritis	Right elbow	Few weeks	6/ 8/37	4	Č
	A.D.	M	60		Spondylitis	Lumbosacral	10 years	6/ 8/37	8	C
			35	Printer	Spondylitis	Lumbosacreiliac	Few months	6/17/37	6	C
	S.W.	M	38	Salesman	Spondylitis	Cervicodorsal	3 years	-6/17/37	7	Imp
	L.H.	F	35	Saleslady	Spondylitis	Cervicodorsal	2½ weeks	6/24/37	7	C
28	L.N.	M	60	Butcher	Arthritis	Left sacroiliac and knee	Few years	7/ 6/37	Three courses	Imp
29	M.B.	M	45	Physician	Calcified bursitis	Subdeltoid	Few days	7/ 7/37	7	C
30	M.M.	M	25	Salesman	Bursitis	R. shoulder	5 months	$\frac{7}{16} / \frac{3}{37}$		č
3 I	R.G.	$\mathbf{F}$	34	Housewife	Spondylitis	Cervical	4 months	$\frac{7/10/37}{7/28/37}$	• 6	Č
	B.W.	M		Physician	Spondylitis	Lumbar	Few years			
	M.G.	M		Executive	Spondylitis	Cervical		8/10/37	8	Imp
	M.S.	F		Saleslady	Spondylitis Spondylitis		Few months	8/10/37	8	Imp
			33	Salesiady	Arthritis	Cervicodorsal R. sacrolliac	2 months	8/19/37	10	Imp
		F		Housewife	Spondylitis	Cervical	4 months	8/28/37	9	Imp
				Housewife	Arthritis	Knee and ankle	Few months	9/ 3/37	3	Imp
37	S.M.	M	35	Truckman	Arthritis	Sacroiliae	4 months	9/ 7/37	10	Imp
8	M.K.	$\mathbf{F}$	60	Housewife	Spondylitis	Cervical	4 weeks	9/18/37	8	Imp
9	I.R.	M	42	Physician	Bursitis	Shoulder	Few weeks	3/10/37	4	Imp
	B.G.	$\mathbf{F}$		Housewife	Metatarsalgia	Great toe	1 year	$\frac{3}{10}$ , $\frac{3}{34}$		C
	J.W.	M	***	Butcher	Spondylitis	Lumbar	8 years		3	C—R
			,		Arthritis	Sacroiliac	•	12/14/34	9	
			41	Butcher	Spondylitis Arthritis	Lumbar Sacroiliae	1 week	6/21/35	7	С
		$\mathbf{M}$	39	Laborer	Spondylitis	Lumbosacral	4 weeks	10/26/37	4	Imp?
3	M.K.			Housewife	Spondylitis	Cervical	5 weeks	1/10/38	5	Imp
4	M.T.		*	Grocer	Arthritis	Sacroiliac	9 months	$\frac{1}{10}, \frac{36}{38}$	14	Imp
-			4.7	Watchman	Arthritis	Sacroilize	2 months	$\frac{2/1}{38}$	-	С
				Housewife	Bursitis	Shoulder	5 days		4	č
•				Housewife	Arthritis	Sacroiliac		2/23/38	6	
				Housewife	Osteo-arthritis	Knee	2 years	3/ 8/38	6	C
				Housewife			9 months	3/15/38	8	Imp
	_		•		Arthritis	Shoulder	2 years	3/16/38	10	Imp
				Hat-blocker	Spondylitis	Dorsal	2 years	3/18/38	2	Imp
		CVE	50 .	Storekeeper	Spondylitis	Lumbar	5 weeks	4/ 1/38	8	Imp
[ ]				TS	TEA.	COL 1.5	-			
1 l 2 ]	I.G.	M	49	Dentist Presser	Bursitis Bursitis	Shoulder Calcified sub-	4 weeks	4/16/38 6/ 7/38	4	C

TABLE I-	-Continued
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Case	Name	Sex	Age	Occupation	Diagnosis	Part Affected	Duration	Treatment Began	No.	Result
154	E.G.	F	50	Housewife	Bursitis	Subacromial	2 weeks	5/27/38	6	Imp
155	M.W.	M	55	Physician	Spondylitis Arthritis	Lumbar Sacroiliac	4 weeks	5/28/38	5	Imp
156	P.K.	M	60	Physician	Spondylitis Bursitis	Cervical Calcified sub- deltoid	5 amonths	7/21/38	8	С
57	B.F.	F	55	Housewife	Bursitis	Subacromial	3 months	7/25/38	12	Imp
58	M.M.	$\mathbf{M}$	45	Business	Bursitis	Subdeltoid	2 weeks	8/ 2/38	2	C '
59	B.B.	M	54	Physician	Spondylitis Bursitis	Cervical Subdeltoid	8 months	8/ 8/38	5	Imp
60	C.A.	M	43	Antiques	Spondylitis	Cervical	1 month	8/ 8/38	5	Imp
61	S.P.	F	34	Housewife	Spondylitis Bursitis	Cervical Calcified sub- deltoid	I week	8/11/38	2	Imp?

sometimes a slight rise in temperature. These reactions may follow a few hours or a few days after the treatment is started. Sometimes no reaction takes place until the second or third treatment. Some patients experience no ill effects, whereas in others the reactions may be quite severe and may last from one to three days. I have found that the chronic cases are more apt to be followed by reactions than the acute.

With experience it is possible to predict whether a case will respond favorably to the treatment, and one may venture an opinion as to the number of treatments necessary to alleviate the condition. For instance, if a definite subdeltoid bursitis with associated excruciating pain and tenderness is referred for treatment and I find reentgenological evidence of calcification in the region of the bursa, I can say with reasonable certainty that the patient will respond. Again, a case of spondylitis in which there is present lipping of the bodies of the vertebrae with pain and tenderness in this region always yields to high voltage roentgen therapy.

#### RESULTS

As indicated in the table, the large majority of the patients were completely relieved of pain and remained free of symptoms. Several patients had one or more recurrences and were relieved by a repeated course of treatments. A few did not respond to this form of therapy. A number of cases

who were coentgenographed again showed complete absorption of the calcified foci with disappearance of symptoms. For various reasons many of the cases could not be followed up roentgenographically.

#### REPORT OF CASES

The following are illustrative cases:

Case 2. J. W., male, aged forty-two, was referred by his physician on April 26, 1932. The patient had pain in his right shoulder for several months. For the past few days the pain had become excruciating and radiated down the right upper extremity to the fingers. He was unable to move his arm and could not sleep on account of the pain, which was not affected by morphine. Roentgenographic examination of the right shoulder showed a large calcified subdeltoid bursitis. After one treatment the pain subsided, the patient began to move his arm and slept through the night. A second treatment was given two days later and was followed by complete recovery.

Case 47 J. N., female, aged sixty-five, mother of a physician, is another similar example of calcified subdeltoid bursitis. The patient had pain in the left shoulder for three weeks, which became so agonizing that it could not be controlled by hypnotics. The first treatment believed the patient and the pain disappeared entirely after three treatments.

Case 129, M. B., male physician, aged fifty, had a calcified subdeltoid bursitis (Fig. 1) which was associated with severe pain. Following treatment the pain disappeared and nine weeks later roentgenographic examination



Fig. 1. Case 129. July 7, 1937. Calcified subdeltoid bursitis.

showed complete absorption of the calcified focus (Fig. 2).

Case 64. L. Z., male, aged forty-five, was referred on April 22, 1935, with a history of pain in the neck, radiating to the left shoulder and down the left arm. This condition had existed for twenty-six days. Diathermy and various other forms of therapy did not relieve the pain. Roentgen examination revealed the presence of a marked spondylitis involving the third, fourth, fifth and sixth cervical vertebrae. After five treatments the patient was free of symptoms.

Case 63. A. W., female, aged fifty. On April 18, 1935, she had been complaining of pain in the anterior subcostal region for more than four years. During this entire period she was

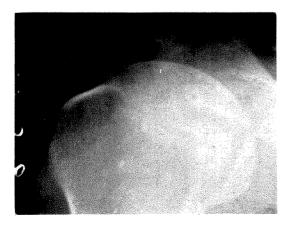


Fig. 2. Case 129. September 8, 1937.
After treatment.

never free from pain, was incapacitated and was unable to pursue her occupation. She tried various forms of therapy; spinal fusion was suggested and considered. Roentgen examination revealed the presence of a dorsal spondylitis (hypertrophic osteo-arthritis) with associated lipping of the bodies of the thoracic vertebrae. It was necessary to give eleven treatments before obtaining satisfactory results.



Fig. 3. Case 152. April 16, 1938. Calcified subdeltoid bursitis.

CASE 141. J. W., male, aged forty-one. The present condition started eight years ago when the patient attempted to lift a rowboat; he experienced a pain in the lumbar region, which persisted. During the past two months the pain became more severe and passed down his right thigh interfering with walking. Roentgen examination showed the presence of a lumbar spondylitis and bilateral sacroiliac arthritis. The patient was given nine treatments and was completely relieved. He had a recurrence

six months later and received seven more treatments with successful results.

Case 21. J. C., female, aged forty, the wife of a physician, had an extraction of an upper molar followed three days later by excruciating neuralgic pain on the same side of the face. The dentist called it a "dry socket" and was unable to control the pain with hypnotics. She received one treatment and was completely relieved. Two days later, following a four hour session in a beauty parlor, the pain recurred.

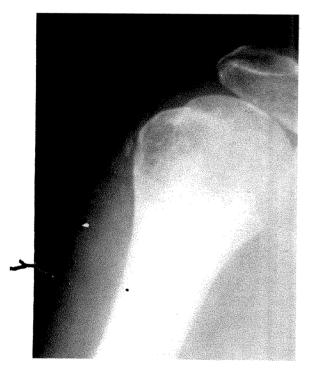


Fig. 4. Case 152. April 22, 1938. During treatment.

Another treatment was given, followed by complete recovery.

Case 140. B. G., female, aged thirty-two, wife of a physician, was roentgenographed for pain in the left great toe of one year's duration. Only a congenital bifid sesamoid on the plantar surface of the great toe was found. No distory of trauma existed. She had great difficulty in walking. During her suffering she had tried various orthopedic shoes and appliances and obtained no relief. Her condition was diagnosed metatarsalgia. Three treatments caused complete and permanent disappearance of pain.



Fig. 5. Case 172. May 4, 1938. During treatment. She now walks and dances without any difficulty.



Fic. 6. Case 152. May 28, 1938. At end of treatment.

#### CONCLUSIONS

The cases from which I draw my conclusions were referred by practicing physicians who, as a rule, exhausted all other orthodox and standard forms of treatment before trying roentgen therapy. I had the opportunity to follow up the majority of these patients through the courtesy of their family physicians, some for a period of five or six years. The results obtained certainly justify continuation of this form of therapy in para-arthritis associated with pain. The fact that a scientific basis of roentgen therapy in these conditions is not definitely established is no reason for discarding this form of treatment.

Some of the explanations given for the effect of the treatment are: (1) roentgen rays have an analgesic effect; (2) roentgen

rays have a direct effect on lymphocytes and leukocytes and reduce general inflammation and pressure on the nerve sheaths; (3) roentgen rays produce a better blood supply in a diseased area through its effect on the vegetative nervous system with a consequent better tissue metabolism.

#### REFERENCES

- 1. Sokolow, Vrach, 1897.
- 2. STENBECK. Paper before the Nord. Kong. f. inn. Med., 1898.
- 3. Anders, Daland and Pfahler, G. E. Treatment of arthritis deformans with the roentgen rays. 7. Am. M. Ass., 1906, 46, 1512-1514.
- 4. Langer, H. Roentgentherapy in arthritis. Radiology, 1933, 20, 78-84.
- 5. DE LORIMIER, A. A. Roentgen therapy in acute para-arthritis. Am. J. Roentgenol. & Rad. Therapy, 1937, 38, 178-195.



# ROENTGEN THERAPY OF BILATERAL PAROTID FISTULA\*

By ROBERT J. REEVES, M.D. DURHAM, NORTH CAROLIFA

UNILATERAL salivary fistulae are not uncommon, but bilateral fistulae as a surgical complication are considered quite rare.

Barbera<sup>1</sup> made a critical study of the several operations for salivary fistula and concluded that the suppression of salivary secretions was best produced by high voltage roentgen irradiation, directly on the parotid gland. His technique was as follows: focal distance, 30 cm.; hardness of rays, 180 kv., and filtration of rays through 0.5 mm. copper and 3 mm. of aluminum. The total dosage was 600 roentgens, measured on the skin, given every other day as follows: 300 r followed by 150 r each for the second and third treatment. He found the salivary secretion controlled from the first roentgen treatment. After the third and last treatment, it was definitely suppressed. The fistula was found to heal in two or three days after completion of the treatmeet. He reported one case in which satisfactory results were obtained by irradiation. Our experience is also limited to one case. Our case did not respond as well as that of Barbera in that it required a larger number of treatments. This may be due to the fact that we were using a shorter wave length but chose to do so because the patient was very fair and the latent skin changes were to be avoided.

#### CASE REPORT

White female, aged thirteen, came to the hospital July 7, 1936, complaining of bilateral fistulae of eight years' duration.

Past History. Contracted measles at the age of three. The tonsils and adenoids were removed at three and one-half years. On February 26, 1930, at the age of six, she contracted

<sup>1</sup> Barbera, G. Roentgen treatment of salivary fistula. *Policlinico* (sez. prat.), 1936, 43, 1773–1776.

tive. Six weeks later, the cold was better. The adenoids were again removed. Both ears became abscessed and were opened. The temperature at this time became spiking in character and at times reached 106° F. Blood cultures were positive for hemolytic streptococcus. Roentgenograms of both mastoids showed suspicious evidence of disease and on April 20, the patient was admitted to the Baltimore Ear, Nose, and Throat Hospital, and a bilateral mastoidectomy was performed. The temperature remained spiking in character. The left ankle became swollen and was opened and drained Lepeated blood transfusions were given. The heart at this time showed evidence of endocarditis. The fifth week after mastoidectomy, the left hip was opened and drained. Transfusions were given at intervals of four weeks. Blood cultures during this time became negative. The joints showed less inflammation and cleared up rapidly. The mastoid incisions continued to drain, and in August the patient was disharged from the hospital. At this time, saliva was found coming through the bilateral fistula. There was a steady flow when eating and a small amount between meals. This drainage has persisted for seven years.

a cold with cough, which lingered in spite of

medical attention. A tuberculin test was nega-

Physica examination at the time of admission was entirely negative except for a small parotic fistula 2 cm. below the middle ear on either side. Marked salivation was noted after chewing gum.

Lipiodal injection disclosed sinus tracts extending ir to the inferior ducts of both parotid glands

Roentgen therapy was begun, using 200 kv., Thoraeus filter, and 300 r, measured in air, at two week intervals, to alternate sides. A 3 cm. sc. field was used, shielding the major portion of the parotid gland. A total of 1,800 r was giver to each side. Examination on January 9, 1537, showed both sinus tracts closed and no further discharge has been noted.

<sup>\*</sup> From the Roentgen-Ray Department of Duke University Hospital and Medical School.

## PERIPHERAL NERVE DESTRUCTION

## AN UNUSUAL SEQUEL OF RADIUM THERAPY

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ana

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THE radioresistance of nerve tissue, particularly the fibrils of peripheral nerves, is well known. A review of the literature fails to reveal any report of nerve

#### CASE REPORT

M. C., aged fifty-eight, married, was admitted on April 27, 1936, with a growth on the left side of the forehead of three months' dura-



Fig. 1. Appearance of lesion before therapy.

Fig. 2. Appearance of lesion at present writing.

Fig. 3. Frontal view showing paralysis of left frontalis muscle and edema of periorbital tissue.

destruction as a result of irradiation without massive tissue necrosis. In our experience in the treatment of epithelioma of the skin at the Brooklyn Cancer Institute with roentgen rays or radium, we have never encountered a similar instance of nerve destruction following therapy. tion, associated with slight pain and occasional bleed ng. She also gave a history of having had a 'sore' on her face twenty-three years ago which, she said, was treated by roentgen ray.

Examination on admission revealed an indurated mass 3 cm. in diameter on the left ten ple with the central portion ulcerated. The left cheek was the site of a pale scarred area,

apparently healed remnant of the old lesion.

Roentgen examination of the skull on May 19, 1936, showed no bone involvement. Wassermann reaction was negative. Biopsy was reported as basal cell epithelioma.

On May 18, 1936, four platinum needles with filtration of 0.5 mm. were inserted for forty-eight hours with a total dose of 1,500 mc-hr.

On March 1, 1937, lesion was reported as clinically healed.

On May 18, 1937, over the area of the treated lesion, a small subcutaneous nodule 1½ inches lateral to the external canthus was felt. Biopsy of this lesion was reported as basal cell epithelioma, and treatment was again given, on June 3, 1937, with four platinum needles for dosage of 800 mc-hr.

On July 15, 1937, lesion was again described as well healed.

On October 28, 1937, again an acorn-sized hard mass was palpable at the posterosuperior angle of the scar. Roentgenogram of the skull showed no bone involvement.

On November 9, 1937, again four needles were inserted for forty-eight hours with total dosage of 800 mc-hr.

dosage of 800 mc-hr.

On November 27, patient appeared with the usual marked irradiation reaction over the treated area and also complained of severe par over left temple and supra-orbital region. The nodule described was no longer palpable. She presented at this time a rather marked edema of the left supra-orbital region, upper and lower left eyelids as well as a paralysis of the left frontalis muscle fibers as evidenced by inability to raise the left eyebrow. There was no disturbance of sensation. This paralysis and edema have persisted up to the present, without any change.

The paralysis came on during the course of the irradiation reaction. The latent

period of one week between the application -removal of needles and the onset of paralysis—would rule out any mechanical injury to the nerve by the radium needles. Any puncture would have been followed immediatel by paralysis. The fact that pain preceded the onset of the paralysis would indicate an inflammatory change in or around the nerve which, with the appearance of palsy, had apparently progressed to complete interruption. The destruction of the nerve by neoplastic invasion could be ruled out by the disappearance of the nodule treated concomitantly with the onset of paralysis. The edema of the periorbital tissues is attributable to virginatic obliteration by the irradiation effect. There was no external ulceration as time site of needle application, indicating that no unusual amount of radium had been applied.

The presence of considerable scarring at the site of the lesion from previous therapy might indicate a pre-existing fibrotic band constrict in the nerve bundle. The addition of new radiation reaction with its inflammatory edema may have increased the degree of constriction to final obliteration of the nerve by kinking or stretching; a condition similar to the ulnar nerve paralysis seen as a late sequel of fractures of the lateral epicoadyle of the humerus. This late complication, that is secondary obliteration of nerves and lymphatics by scar tissue, should be anticipated in applying intensive therapy to areas containing these structures. We do not believe the paralysis was a circuit result of irradiation on nerve tissue itself.



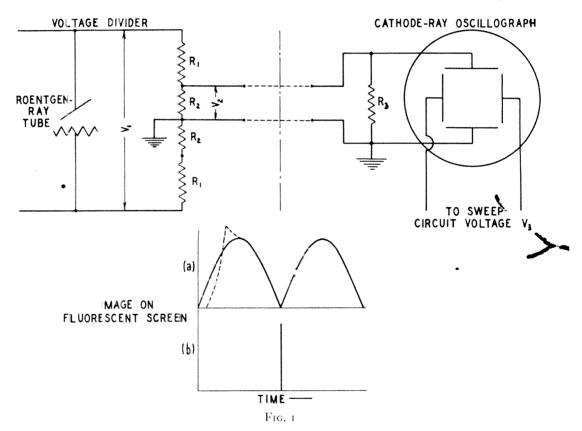
# THE USE OF THE CATHODE-RAY OSCILLOGRAPH\* FOR MEASURING ROENTGEN TUBE VOLTAGE†

Ey CHARLES WEYL, S. REID WARREN, JR., and DALLETT B. O'NEILL PHILADELPHIA, PENNSYLVANIA

IT HAS long been recognized that the roentgen tube voltage calibration of roentgenographic and roentgen therapeutic apparatus may be obtained most accurately by means of a high resistance voltage divider and an oscillograph. Formerly, the apparatus required has been expensive and

#### THEORETICAL DISCUSSION

In Figure 1 is shown the schematic wiring diagram of the essential components of this system. Two high resistances  $R_1$  in series with two lower resistances  $R_2$  are connected across the roentgen tube. The midpoint of these series resistances is grounded.



its use has necessitated exposing and processing an oscillographic film for each measurement. Recently, commercial development of inexpensive high value resistors and a cathode-ray oscillograph have made the cost of this apparatus comparable to that of a good sphere gap. This apparatus and its use are described below.

In this way, a voltage  $V_2$  is obtained across one of the smaller resistances  $R_2$ . This voltage  $V_2$  is proportional to the roentgen tube voltage  $V_1$ .

The cathode-ray tube shown on the right has a fluorescent screen upon which impages a beam of high velocity electrons. The image is produced by this beam strik-

<sup>\*</sup> If the instrument is used to observe wave forms visually, it is properly called an oscilloscope, but commonly called an oscillograph.

† The work described has been conducted at the Moore School X-rey Laboratory of the University of Pennsylvania under grants from L. J. and W. Rosenwald, the University of Pennsylvania, and the National Tuberculosis Association.

ing the screen and the beam is caused to deflect by means of voltages across the two pairs of plates. The voltage  $V_2$  is applied across the vertical deflecting plates, cansing the electron beam to move up and down. A separate voltage  $V_3$  is applied to the horizontal deflecting plates. This voltage varies in such a manner that the beam travels across the screen at a uniform welocity from left to right. When it reaches the right hand side it moves back to its starting position instantaneously and repeats its travel. The resistance  $R_3$  shown across the vertical deflecting plates is usually found so connected in commercial cathode-ray oscillographs.

Since the sweep circuit voltage  $V_3$  causes the electron beam to move across the screen uniformly from left to right and the applied voltage V<sub>2</sub> causes it to move vertically at the same time, the resultant image represents the wave form of  $V_2$ , as shown by the solid line in Figure I(a). If the period of  $V_3$  is so adjusted that the beam moves agross the screen in one cycle of  $\mathbb{Z}_2$ then the image of each succeeding cycle of  $V_2$  is superposed upon the preceding images. I the oscillograph has been calibrated, the vertical deflection at any instant is a mezsure of the magnitude of  $V_2$  at that instant. It is then possible to calculate the magnitude of  $V_1$  from the measured value of  $F_2$ .

#### HIGH RESISTANCE VOLTAGE DIVIDER

The high resistance voltage divider used for these measurements must satisfy the following requirements:

- (1) It shall impose no appreciable load on the high tension generator.
- (2) It shall have low inductance and capacitance so that the wave form will not be distorted. This is particalarly important for the observation of transient phenomena.
- (3) The values of the resistors must remain constant over long periods of time under the conditions of varying temperature and humidity encountered in roentgen-ray laboratories.

- (4) It shall be easily connected to the high tension conductors.
- (5) It shall be portable.

Two types of high value resistors have been employed which satisfy these requirements.

The first was designed for use with roentgenographic apparatus haring roentgen tube voltages up to 100 kv (peak). This voltage divider is shown in F gare 2 (upper). The bank of resistors comprises 100 International Resistance Company Type BT-1\* one megohm units for  $R_1$  and two IRC BT- $\frac{1}{2}$ 100,000 chm units for  $R_2$ . These resistors are mounted as follows: There are six bakelite tubes ezch 23 inches long and 7/16 inch outside diameter. The inner bore of the tube is sufficiently large to take the BT-1 units and leave an annular space between the outside of the unit and the inside wall of the order of 1/32 of an inch. Each resistor consists of a piece of glass tube about 0.04 inch in diameter with two No. 20 tinned corper leads attached to the resistance coating of the glass tube; this assembly is then moulded into a cylindrical piece of bakelite in such a manner that the leads extend axial from each end of the cylinder. Theone megohm units may be ordered with a tolerance of plus or minus 10 per cent. This reduces the cost of the resistors considerably. When the units are received each unit is measured on a Wheatstone bridge and the 100 units divided into two groups such that the resistance of the first group is equal to I per cent or less of the resistance of the second group. One group of resistors is then divided into three parts in the following manner:

- (1) Seventum resistors with a total resistance of approximately 17 megohans;
- (2) Seventien resistors with a total resistance of approximately 17 megohas;

<sup>\*</sup> The apparatus \*\*escribed here and elsewhere in the paper is that which has been seed by the authors. It is probable that similar apparatus of other manufacturers can be adapted to perform the same functions

(3) Sixteen resistors with a total resistance of approximately 16 megohms and one 100,000 ohm unit.

Each of the first two groups of 17 resistors is then arranged in a straight line, the pig-

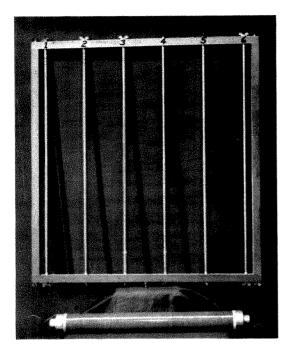


Fig. 2

tails cut so that their total length is about 1 inch and the whole series soldered together with due care that the total length of the 17 units soldered together does not exceed the length of one of the bakelite tubes. This series of resistors is then slipped into one of the bakelite tubes and a brass piece is fastened to each end of the tube. The lead to each end of the series is soldered to one of these brass fittings. The third tube for this part of the resistance bank is like the other two except that a small hole is made in the tube about  $1\frac{1}{2}$ inches from one end in order to bring out the lead from that end of the 100,000 ohm resistor which is connected to one of the I megohm resistors. Finally, four pieces of <sup>3</sup>/<sub>4</sub> inch square linen base yellow bakelite are assembled to form a square frame, the inside dimensions of which permit the mounting of the six tubes with approximately 4 inches between each two tubes. The frame and the resistors are held together by means of wing nuts. Strips of sheet brass are used to connect the six sections in series. These strips are placed along the bottom surface of the framework to connect sections 1 and 2, sections 3 and 4, and sections 5 and 6. They are placed along the top surface of the framework to connect sections 2 and 3, and sections 4 and 5.

This voltage divider has been in use for a period of approximately three years. It has been used on short exposures only to prevent overheating of the resistance units. Under these conditions the total resistance of this 100 megohm unit has changed about 2 per cent.

The second type of voltage divider can be used for both roentgenographic and toentgen therapeutic appartaus. It has been used up to voltages of 200 kv. (peak). The lower value resistors  $R_2$  are of the BT-type with resistance of 400,000 ohms each. The two high resistance units are International Resistance Company type MRV and each has a value of 200 megohms. One of these is shown in Figure 2 tlower).

#### CATHODE-RAY OSCILLOGRAPH

The cathode-ray oscillograph to be used for these measurements must satisfy the following requirements:

- (1) The vertical deflection must be proportional to applied voltage.
- (2) The fluorescent screen must be of the long persistence type to provide adequate time for observation on short exposures.
- (3) The calibration of the vertical deflection must be constant under conditions of line voltage variations of  $\pm$  10 per cent.
- (4) It must be possible to control the intensity and focusing of the electron beam and the magnitude and frequency of the sweep circuit voltage.

While it is possible to build an oscillograph satisfying these requirements it has been

found advantageous to use one of the commercial models now available. These commercial oscillographs are inexpensive and can be used for other purposes.

The cathode-ray oscillograph which has been used is the RCA type TMV122C which operates on 25 or 60 cycles. If operation on 60 cycles only is necessary type TMV122B may be used. The cathode-ray tube is the RCA type 910 which has a long persistence fluorescent screen. In some oscillographs the leads from the vertical deflecting plates are brought out to pin jacks on the panel. In the particular model used it was necessary to bring these leads out separately. This is easily accomplished by removing the case of the oscillograph and soldering the leads directly to the cathode-ray tube socket terminals. Because of the high voltage of the power supply unit in the oscillograph, it must not be operated until the case has been replaced.

In order to assure constancy of calibration on various supply lines a 60 watt Raytheon type VR2 voltage regulator was used. This voltage regulator operates on a constant frequency (60 cycles/sec.) input voltage from 95 to 130 volts. The oscillograph is operated from the output voltage of the regulator, the rms value of which is 115 volts ±1 per cent. The cathode-ray oscillograph and stabilizer are shown in Figure 3.

#### METHOD OF USE

The high resistance voltage divider and and cathode-ray oscillograph are connected as shown in Figure 1. A 45 volt battery and a voltmeter are connected across the input to the vertical deflecting plates. The magnitude of the deflection on the screen is measured with a pair of calipers. This permits the calculation of the calibration constant K since  $V_2 = Kd$  where d is the deflection of this spot on the fluorescent screen. This relationship should be checked at several values of  $V_2$  to make certain that the deflection is proportional to applied waltage.

The current through  $R_1$  is

$$I = \frac{V_1}{2R_1 + R_2 + \frac{R_2R_3}{R_2 + R_3}}$$

The same current flows through  $R_2$  and  $R_3$  in parallel and is

$$\tilde{f} = \frac{V_2}{R_2 R_3}$$

$$R_2 + R_3$$

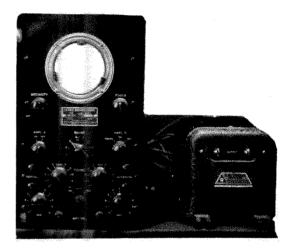


Fig. 3

Equating the two values of I there is obtained

$$F_1 = \left(\frac{(2R_1 + R_2)(R_2 + R_3)}{R_2 R_3} + 1\right) V_2$$

From the calibration of the oscillograph

$$V_1 = \left(\frac{(2R_1 + R_2)(R_2 + R_3)}{R_2 R_3} + 1\right) Kd$$

To measure the roentgen tube peak voltage the sweep circuit voltage  $V_3$  is reduced to zero. The resulting image during an exposure is a vertical line, as shown in Figure I(b), the keight of which may be measured with the calipers, giving a value for d. The exposure time for this measurement should be I/20 second or more to provide sufficient brightness of the image. If the measurement is made in a room having low illumination or with a hood over the front of the cathode-ray oscillograph the image will persist for the ray to sixty seconds.

In order to observe the wave form of the roentgen tube voltage the magnitude of  $V_3$  is adjusted to provide a horizontal deflection just slightly less than the width of the cathode-ray tube. The period of  $V_3$  is adjusted to move the spot across the screen once every cycle of  $V_2$ . In this way, each cycle of  $V_2$  is superposed and a bright image of the wave form will result. If the timer on short exposures does not start or end on zero there will be noted on the screen images which do not coincide with

the normal wave form as shown by the dotted line in Figure I(a).

In order to use the cathode-ray oscillograph for checking the exposure time the period of  $V_3$  is increased so that the spot moves across the screen in a longer time than is produced by the timer. Each half-cycle of roentgen tube voltage may then be seen separately and counted. It is necessary that the sweep period be greater than the exposure time to avoid any superposition of half-cycle images.



### THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Delegates the Sixth International Congress of Radiology: Albert Sciland, Los Angeles, Calif., Delegate, Zoe A. Johnston, Pittsburgh, Pa., Alternate Delegate.

Twenty-fift: Amenal Meeting: New York City, June 10-11, 1994C.

#### ∞ E D I T O R I A L S ∞

# AIR INJECTION IN THE ROENTGEN DIAGNOSIS OF CORTICAL AND MEDULLARY TUMORS

IIIH the widespread use of the Potter-Bucky diaphragm as an aid in roentgen diagnostic procedures, the employment of gases as contrast media in the peritoneal cavity has fallen somewhat into disuse though in selected cases they still have a very distinct and definite place. Shortly after the announcement of the use of gases in the peritoneal cavity as contrast media, a number of observers independently called attention to the improved visualization of the kidney by the retroperitoneal injection of oxygen or carbon dioxide and this method of examination of the perirenal space assumed very shortly considerable diagnostic importance. While most observers called attention to the ease with which the adrenal glands might be visualized by this procedure, it was not antil Mosenthal and Löser and Israël emphasized the importance of perirenal retroperitoneal insufflation of air as an aid in the diangosis of enlargement of the adrenal glands that there was a revival of interest in this procedure. This revival of interest came at the time when the adrenal glands were being investigated as an etiological factor in some of the obscure clinical syndromes.

Quite recently Cope and Schatzki<sup>1</sup> have called attention to the importance of perirenal retroperitoneal insufflation of air as a diagnostic aid in tumors of the adrenal glands. Their study is based on 163 separate injections of air in 78 patients. In all of their cases studied there was some clinical reason to suspect disease of the adrenal glands. The size of the shadows outlined by air visualized on the roentgen film was con-

firmed by operative exposure through a retroperitoneal approach in 15 patients and by postmortem examination in two patients.

A great deal of the success of the inject on of air into the perirenal space is due to the technique of the procedure, and Cope and Schatzki have given in detail the technique which they have followed in all of the cases studied. The site of choice for injection of air into the perirenal space is the triangular fat pad below the kidney. The lower pole of the kidney rests in a mass of fat which lies between the anterior and posterior folds of renal fascia above the pelvic brim. The presence of a ptotic kidney should first be excluded by palpation or by roentgen examination. They call attention to the meticulousness with which the technique should be followed in order that the best results may be achieved and also to obviate the occurrence of any untoward symptoms.

Not only the site of the injection but the depth to which the needle passes and the volume of the injection together with the rate of injection and the pressure used are of importance in the success of the procedure.

Cope and Schatzki call attention to the technique which they used in avoiding certain possible complications, namely, air embolism, and the possibility of the insertion of the needle into the kidney substance producing a hematoma of the renal capsule and also the avoidance of passing the needle into the adrenal gland itself thereby producing a hematoma of this gland. The danger of these complications is considerably lessened by introducing the needle at the site as selected by Cope and Schatzki,

<sup>&</sup>lt;sup>1</sup> Cope, Oliver, and Schatzki, Richard. Tumors of the adrenal glands. 1. A modified air injection roomgen technic for demonstrating cortical and medullary tumors. *Arch. Int. Med.*, 1939, 64, 1222-1238.

namely the lower rather than the apper portion of the renal space. With the low pressure and the slow rate of injection of the air pain is minimized. Following the injection of the air the patient is asked to walk around for at least half an hour. They have found it unnecessary in their technique to massage the loin. In the majority of cases a complete diffusion of the air and better visualization of the organs were obtained after twenty-four hours. It is their practice to take one set of films withir an hour after the injection and a second set twenty-four hours later; anteroposterior and lateral views are taken at each time. It is unnecessary to have any special preparation of the gastrointestinal tract except that the colon should be clean. They lave found it advantageous in a study of the lateral films to inject the air on one side at a time and they have allowed a week to elapse between injections. In this length of time practically all of the air previous iniected has been absorbed. In their saudy they found that the normal adrenal gland is not always visualized on the roentenograns after the injection of air; however, when outlined in its variety of shapes it conforms closely to the gross anatomy of the adrenal gland as seen at operation or autopsy. The left gland is generally elongated; the right, pyramidal.

One difficulty of interpretation is caused by superimposed irregular shadows cast by the fat and connective tissue surrounting the gland. The density of the shadow cast by the normal adrenal gland is ordinarily greater than that cast by surrounding tissues but is of less density than the upper pole of the kidney.

In their experience the anteroposterior films give the most satisfactory results and they have in some of their studies used intravenous pyelographic media simultaneously with the air injection.

This method of examination is of considerable importance in the visualization of small tumors not shown by other means and it is is also of value in the exclusion of the adrenal glands as the primary scurce of

disease by demonstrating normal gland shadows. It is an aid in demonstrating bilateral hyperplasia of the adrenal glands and in the cifferential diagnosis of shadows in the per renal area which have been mistaken for sumors of the adrenal glands.

In commenting upon the usefulness of such a procedure, Cope and Schatzki call attention to the dangers which may follow the injection of air into the perirenal spaces or into the body cavities, but with the safeguards which they have outlined they believe it is a method which can be used on an ambulatory patient. In the 163 separate injections there have been no fatalities and no signs of air embolism. The only complications in their series occurred in the first twent\* cases in which the site of injection recommended in the literature was used. They emphasize an important point in their technique, namely, that there is such a variation in the anatomy of the individual patients that no actual measurements so far as depth to insert the needle is concernec can be followed. One must perforce have surgical judgment in utilizing such a procedure rogether with a complete knowledge of the anatomy and above all the position of the needle itself must be carefully checked before air is injected.

In spite of safeguards, perirenal insufflation is not recommended without reservation and it should be used only in those cases n which there is a definite suspicion of disease of the adrenal glands or tumors in that area. The danger of the method is also noted in a recent report by Weyrauch of a case in which death occurred from air embolism following perirenal insufflation.

The modified technique of Cope and Schatzsi tends to lessen the dangers in the employment of this method for the diagnosis of per renal tumors and at the same time adds tremendously to our diagnostic armamentarium by enabling us to recognize these tumors earlier in the course of the disease and in certain cases to obviate the necessity of surgical exploration.

<sup>2</sup> Wey-auch, Henry M., Jr. Death from air embolism following perirena insuffication. J. Am. M. Ass., Feb. 24, 1940, 114, 652-653.



HOWARD EDWIN RUGGLES 1886-1939

AT THE height of his meteoric career on December 28, 1939, in his country home near San Francisco, there quietly passed to his rest the "Dean" of Roentgenology of the Pacific Coast, Howard Edwin Ruggles.

He was born in San Francisco and received his Bachelor Degree from Stanford

University in 1907 and his Medical Degree from Harvard Medical School. He returned to San Francisco in 1913 and spent the rest of his life in that city except for the time he so ably served his country as Captain attacked to Base Hospital No. 30 during the World War. His first appointment of roent-genologist to St. Luke's Hospital was

quickly followed by an appointment to the Staff of the University of California Medical School where he rose to the rank of Clinical Professor and head of the Department of Roentgenology. At the time of his death, besides the above mentioned appointments he was Chief Consultant to the Southern Pacific Hospital, Shriners Hospital, Children's Hospital, and the University of California Service at the San Francisco Hospital.

In 1918 he collaborated with his belowed friend and teacher, George Holmes, of Harvard in the publication of a text in roentgenology which has had many editions and is now a standard text for most colleges in America as well as abroad.

In 1936 he collaborated with Miley Wesson in a book on urological diagnosis.

He was a member of the San Francisco County Medical Society, California State Medical Society, the American Medical Association, and of the American Roengen Ray Society which he loyally served as Vice President, member of the Executive Council, and at the time of his death was Chairman of the Publication Committee.

With a rapier-like mind, skillful lands, and a dynamic personality, no man has had a greater influence on the advancement of roentgenology than Howard Ruggles.

He was a master technician and was never content with anything but the best in the diagnostic value of his roentgenograms. His diagnostic ability was uncanny, swift,

and sure, and as a teacher he was unexcelled. The first practical tilting fluoroscope and the Ruggles Sinus Device were children of his brain and he developed one of the earliest methods of successful moving roentgenograms of the heart and that in the days of inefficient tubes, slow screens, and films.

He cared little for competitive games and his only interest in sports was in backing the football team of his alma mater, Stanfo-d, and this he did most strenuously.

His principal hobby was photography and his collection of moving pictures in color of the South Seas excel the professional travelogues and were a source of delight to his many friends.

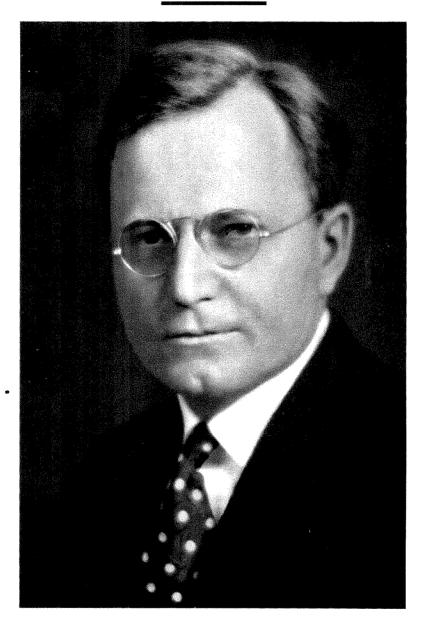
He was always most generous in his aid to the younger medical men and gave many a young rountgenologist his first step up the ladder of success and throughout our land are many prominent roentgenologists who are indebted to Howard Ruggles and to them he is still the "Chief."

The Ligh plane that roentgehology holds in the medical world, particularly on the Pacific Coast, is due in great measure to the inspiration, patience, and untiring energy of Howard.

He wind not in vain. Because of him our profession and our lives are so much richer and fuller that we can have faith that another such as he may come.

LLOYD BRYAN





LOUIS S. WEAVER 1877-1940

In A world where men have done much and have much yet to do, we pause at times to render praise to those who have led in these accomplishments. Today we pause in memory of Dr. Louis S. Weaver, truly a man who accomplished much of work and play and service during his short span of life. The many types of his services

are revealed by his activities. For many years he served on the York Hospital Staff, being Chief Surgeon for the past eight years. He was a charter member of the American Roentgen Ray Society; a member of the American College of Surgeons; past president of the York County Medical Society; past president of the York Medical

Club; past president of the York Lions Club. He was a member of the York Recreation Board; of the York Welfare Board; the York Chamber of Commerce and of the Boy Scout Council. He served six years as a City School Director. A veteran of the Spanish American War and of the World War, he served as Commander of the York Post No. 127, American Legion. He was a regular attendant at Church. He was a trustee of Gettysburg College; and a charter member of his college fraternity, Phi Kappa Psi, in which he was intensely interested. An athlete, he was once City tennis champion.

He worked hard, he played hard. His honesty and his steadfast support of his friends characterized this man. With him, a proposition was either right or it was wrong; one always knew where he stood on all matters requiring a decision. Such an attitude required courage, but brought inward peace. He had a zest for work but did not make gain his god; he remembered the contributions of the past in science and in progress, but he was not enslaved by tradition. He had religious interests, without becoming too far removed from the practical world. His surgical skill, technique, and endurance were recognized by all who knew him.

He Lawes three children, Kathryn, Frank and Louis. His wife, Romaine, preceded limit death several years ago.

We small miss his cheerful manner, his judgment, and his surgical skill. His place will be hard to fill. Our profession truly has lost one of its most distinguished men.

L. S. Landes



#### SOCIETY PROCEEDINGS. CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

#### MEETINGS OF ROENTGEN SOCIETIES\*

United States of America

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. B. Peirce, Royal Victoria Hospital,
Montreal, Canada. Annual Meeting: Hotel Statler, Boston, Mass., Oct. 1-4, 1940.

AMERICAN COLLEGE OF RADIOLOGY

Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Next Annual Meeting: Commodore Hotel, New York City, June 12, 1940.

Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: New York City, June 10-14, 1940. RADIOLOGICAL SOCIETY OF NORTH AMERICA

Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting, 1940: To be announced.
RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SOCIETY

Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September.

Section on Radiology, Illinois State Medical Society

Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill. Next meeting Peoria, Ill., May 21-23, 1940.
RADIOLOGICAL SECTION, Los ANGELES Co. MED. Soc. Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY

Secretary, D. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April. BUFFALO RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host,

CHICAGO ROENTGEN SOCIETY

Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to May inclusive at the Hotel Sherman.

CINCINNATI RADIOLOGICAL SOCIETY

Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, Octo-

ber to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY

Secretary, Dr. H. A. Mahrer, 10545 Carnegie Ave.

Meets at 6:30 P.M. at Mid-Day Club rooms on fourth Monday each month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB

Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY Secretary, Dr. E. R. Witwer, Harper Hospital Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY

Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY

Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

ILLINOIS RADIOLOGICAL SOCIETY

Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, II. Meetings held quarterly, on the fourth Sunday of the month.

Indiana Roentgen Society

Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annuKENTUCKY RADIOLOGICAL SOCIETY

Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville. Meets annually in Louisville on third Sunday afternoon in April.

...n.x.n, 1940

Long Island Radiological Society

Secretary, Dr. Marcus Wiener, 1430-48th St., Brook-lyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS

Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing. Three meetings a year, Fall, Winter, Spring.

Malwaukee Roentgen Ray Society

Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis. Meets monthly on first Friday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY

Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

NEBRASKA RADIOLOGICAL SOCIETY

Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

R-DIOLOGICAL SOCIETY OF NEW JERSEY

Secretary, Dr. W. J. Marquis, 198 Clinton Ave, Newark. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by president.

NEW YORK ROENTGEN SOCIETY

Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society

Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

Central New York Roentgen Ray Society Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November.

PACIFIC ROENTGEN CLUB

Secretary, Dr. L. H. Garland, 450 Sutter St., San Franrisco, Calif. Meets annually, during meeting of Caliornia Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY

Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Next annual meeting, Hershey Hotel, Hershey, Pa., May 17-18, 1940.

PELLADELPHIA ROENTGEN RAY SOCIETY

Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY

Secretary, Dr. H. W. Jacox, 4800 Friendship Ave., Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

RECHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y. Secretary, Dr. S. C. Davidson, 277 Alexander St., Meets on second Thursday from October to May, inclusive, 8 .M., Rochester Academy of Medicine Building.

ST LOUIS SOCIETY OF RADIOLOGISTS Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY

Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

<sup>\*</sup> Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

South Carolina X-Ray Society
Secretary, Dr. Hillyer Rudisill, Jr., Roper Hospital, Charleston. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY

Secretary, Dr. F. B. Bogart, 311 Medical Arts Eldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY

Secretary, Dr. L. W. Baird, Scott and White Hospital, Temple, Texas. Next annual meeting, January 18, 1941, Sherman, Texas.

University of Michigan Department of Roen-cen-ology Staff Meeting

Meets each Monday evening from September to June,

at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference Secretary, Dr. E. A. Pohle, 1300 University Ave., Addison, Wis. Meets every Thursday from 4:00-5:00 F.M., Room 301, Service Memorial Institute.

VIRGINIA RADIOLOGICAL SOCIETY

Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY

Secretary, Dr. K. J. Holtz, American Bank Bldg. Seattle. Meets fourth Monday of each month at the Callege Club, Seattle.

SOCIEDAD CUBANA DE RADIOLOGIA Y FISIOTERAPIA Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

#### BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY

Meets monthly on third Thursday, from November to June inclusive, at 8:15 p.m., 32 Welbeck St., Londor. Section of Radiology of the Royal Society

MEDICINE (CONFINED TO MEDICAL MEMBERS) Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

FACULTY OF RADIOLOGISTS

Secretary, Dr. Barbara M. Key, 32 Welbeck St., London, W.I, England.

Section of Radiology and Medical Electricity, Aus-TRALASIAN MEDICAL CONGRESS

Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

RADIOLOGICAL SECTION OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION

Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussion. CANADIAN ASSOCIATION OF RADIOLOGISTS

Secretary, Dr. A. C. Singleton, Medical Arts Bldg Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S. RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MESSICAL

Association Secretary, Dr. Colin Anderson, Invercargill, New Zea-

#### CONTINENTAL EUROPE

BELGIAN SOCIETY OF ROENTGENOLOGY

land. Meets annually.

Secretary, Dr. J. Boine, Avenue des Ailiés, 134, Lo. vain

Meets monthly on second Sunday at d'Egmonds Palace,

Brussels, except in the summertime.
Sociedad Espanola de Radiología y Electrología Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France

Meets monthly on second Tuesday, except daring months of August and September, 12 Rue de Seine, Earis. Société Suisse de Radiologie (Schweizerische Font-GEN-GESELLSCHAFT)

Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.

Secretary for German language, Dr. Scheurer, Molzgasse, Fiel Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiol-OGIE MÉDICALE

Meetsmonthly on fourth Tuesday, except during month of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radi-OLOGETES EN CZECHO-SLOVAKIA

Secretary, Dr. Walter Altschul, German University, Prague, 1 L52.

DEUTSCHE LÖNTGEN-GESELLSCHAFT (GESELLSCHAFT FÜR RÖNTGENEUNDE UND STRAHLENFORSCHUNG)

Meets armally in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.

Permonent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

SÜD- UND WESTDEUTSCHE RÖNTGENSELLSCHAFT Meets annually in different cities.

Nord- und Osudeutsche Röntgengesellschaft

Meets annually in different cities.

DUTCH SECIETY OF ELECTROLOGY AND ROENTGENOLOGY Holds two meetings a year in Amsterdam, one in the Spring and one in the fall.

SOCIETA TO ETABLE RADIOLOGIA MEDICA

Secretary, A. Fonzio, University of Turin, Prof. Turin Societa Remana de Radiologie si Electrologie Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti Roumania.

Meets second Monday in every month with the ex-

ception of the and August.

ALL-RUSSIAN EDENTGEN RAY ASSOCIATION, LENINGRAD, USSR in the State Institute of Roentgenology and Radio Dgy, 6 Roentgen St.
Secretæræs, Drs. S. A. Reinberg and S. G. Simonson.

Meets annually

LENINGRAD BOENTGEN RAY SOCIETY Secretaries, Drs S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Insti-

tute of Rozningenology and Radiology, Leningrad. Moscow EDENTGEN RAY SOCIETY Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konole)evskv. Meets monthly on first Monday at 8 o'clo₫.

POLISH SOCIETY OF RADIOLOGY

Secretary, Dt. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology Secretary, Dr. B. Krynski, 11 Zielna St.

Meets once a month except in the summertime. Scandingvia & Roentgen Societies

The Scandmavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets ever second month except in the summertime: Society of Medical Radiology in Sweden

Meets in Sockholm.

SOCIETY DE MEDICAL RADIOLOGY IN NORWAY Meets in Calc.

SOCIETY OF MEDICAL RADIOLOGY IN DENMARK

Secretary, Dr. G. Biering, Copenhagen. Meets the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

SOCIETY DE MEDICAL RADIOLOGY IN FINLAND

Meets in Helsingfors. VIENNA ROEKTGE V SOCIETY

Meets first Wednesday of each month, at 6:30 P.M. at Zentra-Röstgen Institut des allgemeinen Krankenhauses Alserstrass 4

JAPAN X RAY ASSOCIATION

c/o Ostaorecic Surgery, Tokyo Imperial University. Meets ar uzly n April.

KINKI R SETTGEN-ABEND SOCIETY

Dr Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi monthly on third Sunday.

#### BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

THE MODERN HOSPITAL AND ITS RELATION TO THE PRACTICE OF MEDICINE

During the past twenty or thirty years there have been rapid and extensive changes in the traditional function of the hospital in its relation to the practice of medicine and the delivery of medical care to the American people.

A much larger portion of sick patients are cared for in the private general hospital today than was the case a generation ago. Out of every dollar spent for medical care in this country approximately twenty-four cents goes to pay a hospital bill, either in private or government hospitals. This represents a cost of about 656 million dollars per year, of which 300 million is provided by taxes, 302 million by patients' fees, and the remainder by contributions and endowments.2 The cost of hospitalization as a result of illness is almost as high as the total cost for private physicians' services during a given year. About 86 per cent of the total families in the United States require the services of a physician in an average year but only 20 per cent of the rotal have at least one hospital case.3 Less than 50 per cent of all family illnesses are hospitalized, vet the costs for hospitalization alone in these cases equals the entire expenditure for all illnesses of the entire family in an average year.4 Half the family bills for illnesses goes for hospital care, but in any one year only one person in fifteen has hospital care.5

The cost of medical care in America, therefore, is very largely a cost for hospital care. That this latter cost is entirely justified is a matter open to serious question. A number of factors has contributed to the

<sup>1</sup> Medical Care for the American People. Committee on the Costs of Medical Care, p. 15.

<sup>2</sup> Economic Problems of Medicine, Christie, p. 61.

<sup>5</sup> Doctors, Dollars and Disease, Foster, p. 15.

increased use of hospitalization and the consequent increased cost of sickness. Many qualified students of the question declare that there is too much hospitalization, anc that many patients subjected to the expensive facilities of the hospital could well be cared for in their own home. Three factors are responsible for this alleged overhospitalization. Doctors have referred their patients to the hospital because it was more corvenient for the doctor to render his services there, patients have demanded that they be admitted to the hospital when they could just as easily have been treated in their homes, and hospitals have encouraged the use of their facilities with an occasional disregard of the need of the patient for those facilities.

Whether deliberately or not, current terdencies on the part of hospitals find their keynote in the first recommendation made by the Committee on the Costs of Medical Care. In 1929 the Committee recommended that medical care be furnished by groups, organized around a hospital.6 Thus the hospital becomes the dominant factor in the delivery of medical services. The importance of the traditional family doctor as the prime figure in an adequate health program is obscured in a trend toward institutionalized medicine with the hospital as the central figure.

Steps toward this goal were made when hospitals began the operation of pay clinics and out-patient departments in competition with the private physician's office. Abandoned was the old concept that out-patient services and part-pay clinics should be maintained only in teaching institutions where patients should be used for clinical material. Further steps were taken when the "middle rate" plan was adopted by a number of hospitals, in which patients were admitted on an adjusted fee basis including not only the hospital bill, but the bill for medical care as well. Other hospitals instituted "flat rate" or "all inclusive" plans under which a patient could

<sup>3</sup> Economic Aspects of Medical Services, University of Chicago

<sup>4</sup> Fundamental Facts on the Costs of Medical Care, Falk, p. 13.

<sup>6</sup> Medical Care for the American People, Committee on the Costs of Medical Care, p. 109.

be admitted to the hospital for diagnostic services and pay a flat fee covering the complete cost for medical services and hospital facilities. Still further and more radical steps were taken when hospitals began the sale of insurance plans which offered as benefits not only the use of the physical facilities of the hospital, but the services of medical specialists as well.

Income from endowments and contituentions was sharply curtailed after 1929. The 7,000 hospitals in this country represent a capital investment of more than 3 billion dollars, with about 22 million added each year for expansion and the interest on these investments plus other fixed charges created a difficult problem in finance. Jospitals began to cast about for some new source of revenue to take the place of decreased endowment income.

Group hospitalization insurance presented itself as a happy solution for the problem, so far as hospitals were concerned. Started as an experiment by one hospital in Dallas in 1927, the idea gained little attention until hospitals began to feel the pinch of depression. Then it began a wide and rapid growth.

Less than 65 per cent of the beds in non-governmental hospitals are normally occupied, yet fixed charges remain about the same regardless of the number of occupants. So even if hospital insurance increased the number of patients, the steady annual income from insurance premiums would provide the new and necessary resenue.

If hospitals had stopped with the establishment of insurance plans for hospitalization there would have been little objection from the medical profession which has guarded so zealously the traditional system of American medicine. But, unfortunately, a number of hospitals went still farther to secure new revenue. Ostensibly operated on a non-profit basis, they began to adopt the rôle of a middle-man in the delivery of cer-

tain medical services to realize a profit on the services of physicians. Out-patient clinics for pay patients began to grow. Hospitals began to compete with private physicians offices. Pathologists and radiologists working in the hospital found themselves competing with themselves in their private offices and with their colleagues. Frequently the department of radiology or pathology was operated in such a manner that a large portion of the fees patients paid for these medical services were diverted into the hospital treasury to meet the interest on building investments and other charges.

Here marks a radical departure in the former position of the private non-profit hospital in the medical picture. Doctors had a was regarded the hospital as a specially equipped hotel where patients, who could not be satisfactorily treated in their own hame could be hospitalized. Now the hospital was beginning an invasion of the medical field, and assuming the position of a commercial entrepreneur by interjecting itself between a doctor and his patient, demanding its portion of the fees passing between the patient and his doctor. Many hospitals collected premiums under insurance contracts providing not only hospitalization but the services of physician, radiologists an 1 pathologists as well.

So the ines of difference were clearly drawn. The medical profession has come to the realization that further encroachments on all types of medical practice are almost sure to follow unless hospitals can be prevailed upon to abandon this unfortunate course, return to the business of hospitalization, and leave the practice of medicine to private physicians.

The recitical profession has long maintained that the institutionalization of medical practice or the application of the principles of socialization would result in a lowering of the quality of medical care available to the American people. Taking cognizance of the gradual trend toward such a cond men through encroachment of hospitals upon the field of private medical

<sup>&</sup>lt;sup>7</sup> Economic Problems of Medicine, Christie, p. 60.

<sup>&</sup>lt;sup>8</sup> Medical Care for the American People, Committee on t e Costs of Medical Care, p. 26.

practice, the Judicial Council of the American Medical Association at the annual meeting in 1936, issued a strong statement to the effect that:

. . . It would seem that in this time of extensive changes in hospital economics the point had arrived at which further marriages between hospitals and staff physicians that make the doctor of medicine the servant of the hospital should be stopped and a series of attempts at divorce among marriages that have already taken place should be instituted. Our accepted ethical principles are adequate at the present time and Hospitals would be of invaluable assistance. It is not an impossible task but will need a militant local and national ethical spirit behind it and a frowning on these individuals in the profession who on personal grounds do not object to the gradual subjugation of the medical profession in the growth of hospital domination.9

## The Code of Ethics of the American Medical Association provides that:

It is unprofessional for a physician to dispose of his professional attainments or services to any lay body, organization, group of individuals, by whatever name called, or however organized, under terms or conditions which permit a direct profit from the fees, salary or compensation received to accrue to the lay body or individual employing him. Such a procedure is beneath the dignity of professional practice, is unfair competition with the profession at large, is harmful alike to the profession of medicine and the welfare of the people, and is against sound public policy.<sup>10</sup>

In this manner the conflicting viewpoints of the medical profession and the hospital group is defined.

The fears of the medical profession in this regard are fully justified by recent statements appearing in hospital publications. These statements evidence a complete disregard of the desires and recommendations of the medical profession. Repeatedly, statements have appeared that hospital service includes radiological, anesthesiological and laboratory services; that the hospital depends upon the profits

from the operation of certain medical departments to maintain the hospital and increase its income; that the services of the clinizian, the surgeon, the pathologist and the radiologist, as well as the nurse, are a part of the hospital and are services to be provided by the hospital free from the dictation of medical men.

Practically all States in the Union have enacted statutes prohibiting the practice of mecicine by corporations. Similar statutes prevail prohibiting the corporate practice of law, dentistry, and other learned professions. These laws have been passed for the simple reason that the practice of the lea-ned professions by artificial legal entities would not be to the best interest or we fare of the people. Hospital corporations are artificial entities and it is hard to un derstand why the same reasoning should noz be applied in their case. The public would surely suffer as the result of this kind of corporate practice the same as it would in the case of non-hospital corporations. The type of organization is relatively immaterial. In any case the traditional and indispensable personal relationship between a doctor and his patient will be destroved or injured under such conditions.

It is true that the authority of the common law is not clear upon the question of the corporate practice of medicine by hospatals. Although important decisions have been rendered by the Supreme Court in several states upholding the statute prohibiting corporate practice, there seems to Le a universal reluctance to apply such rulings to hospital corporations. The law, however, has traditionally lagged at least a generation behind the sciences, and the question involved here is a scientific one and not a legal one. The important point to consider is whether the science of medicine will be preserved and advanced. The general opinion among medical men is that corporate practice, either by hospitals or any other kind of corporation, will hinder the progress of the science and practice of medicine.

The medical profession has found it nec-

<sup>§</sup> J. Am. M. Ass., 1936, 106, 1197.
Principles of Medical Ethics, American Medical Association,

Principles of Medical Ethics, American Medical Association, p. 20.

essary to wage a militant battle against various forces which have during recent years attempted to override the opinion of medical men and bring about revolutionary changes in the form of medical practice in America. In the past the medical profession has looked upon the hospitals as its partner and ally in a relentless fight to preserve the practice of medicine from prejudicial influences.

It will be a great misfortune if the unselfish demands of the medical profession, standing on a firm realization of idealistic principles and scientific truths, be disregarded by a former ally and friend and the hospital shall be found on the side of these dangerous agencies which would substitute their opinions regarding matters of health for the opinions of the doctor.

The threat of hospitals in invading the field of medicine, upsetting the traditional relationships between physician and patient, and supplanting free private enterprise with regimented institutionalization is no less than the threat of other radical forces which the hospitals themselves have denounced.

MAC F. CAHAL

#### AMERICAN BOARD OF RADIOLOGY

The next examination to be conducted by The American Board of Radiology will be in New York City, June 7-9, 1940, but the quota is practically filled for this examination. We would therefore unge those who are anxious to be examined this year to send their applications in immediately so that they may be scheduled for the examination to be conducted in Boston, Massachusetts, September 27-29, 1940.

Address all communications to: Dr. B. Kirklin, Secretary, The American Board of Radiology, Mayo Clinic, Rochester, Minnesota.

Following is a list of those who have been certified or granted additional certification during 1939:

- 1. Abrams Flyr an S., Tuscaloosa, Ala., Radiology
- 2. Ackermann, Affred J., Oklahoma City, Okla., Roentgenol-
- 3. Algin, Sargias, Indiana, Pa., Roentgenology
- 4. Allen, William F., Jr., St. Louis Mo., Radiology
- 5. Almy, Ass & Rochester, N. Y., Roentgenology
- 6. Andrew, F. J., Rochester, N. Y., Radiology
- Anspresser, Aleys G., Macomb, Ill., Radiology
- 8. Athle, Laxin an H., Bombay, India, Radiology
- 9. Bachman, & model L., Stamford, Conn., Radiology 11. Barnes John L., Cincinnati, O., Therapeutic Radiology
- 10. Baltimore, Louis, Los Angeles, Cal., Roentgenology
- 12. Bayliss, Jamb W., Buffalo, N. Y., Roentgenology
  13. Beatty, Sarme R., Denver, Colo., Radiology
- 14. Bell, Charles E., East St. Louis, Ill., Radiology
- 15. Bernssein, Mired J., New York, N. Y., Radiology
- 16. Bersack, Swon on R., Springfield, Mass., Radiology
- 17. Bond Thursas B., Fort Worth, Texas, Roentgenology 18. Bonis, Alexander, New York, N. Y., Radiology
- 19. Boswell, Frederick, P., Montgomery, Ala., Radiology
- 20. Bracker, Cearge J., Seattle, Wash., Diagnostic Roentgenol-
- 21. Bringle, Farry R., Asbury Park, N. J., Roentgenology
- 22. Brown. William L., Sr., Chicago, Ill., Radium Therapy 23. Bryzm. Walkam W., Montreal, Canada, Radiology
- 24. Bug See, Lawn P., Philadelphia, Pa., Radiology
- 25. Bur illa Folmes, E., Philadelphia, Pa., Radiology
- 26. But Et. V Sham J., Providence, R. I., Radiology 27. Carr, Glodys L., Hempstead, N. Y., Roentgenology
- 28. Car ol, William J., Hot Springs, Ark., Radiology
- 29. Casser, Seepaen L., Philadelphia, Pa., Radiology 30. Caulk, Falph M., Washington, D. C., Radiology

- 31. Chang, C. William, New York, N. Y., Radiology 32. Collen, Eard W., New York, N. Y., Therapeutic Radiology 33. Collen, Bea amin, Flushing, N. Y., Diagnostic Roentgenol-
- 34. Conahan, Thomas J., Hazleton, Pa., Radiology 35. Comey James P., Washington, D. C., Radiology
- 36. Coper Seerge, Jr., University, Va., Roentgenology 37. Coper Rosert W., Shreveport, La., Radiology
- 38. Curtzwier, Francis, C., Toledo, O., Radiology 39. Deversa, Joseph J., Brooklyn, N. Y., Roentgenology
- 40. Dell, Maxey, Gainesville, Fla., Roentgenology
- 41. Dolle, Eugene H., Presque Isle, Me., Diagnostic Roent-
- 42. Dowdy, Andrew H., Rochester, N. Y., Radiology
- 43. Editernackt, Arthur P., Indianapolis, Ind., Radiology
- 44. Elliott. William J., Worcester, Mass., Radiology
- 45. Epstern, Bernard S., Brooklyn, N. Y., Radiology

- 46. Farkert, Edwin J., Elkins, West Va., Radiology
  47. Evens. W lliam A., Jr., Detroit, Mich., Radiology
  48. Elerstein, Jacob, New York, N. Y., Roentgenology
  49. Banagan, E. Latane, Richmond, Va., Roentgenology
- 50. Carteriach, Charles, New York, N. Y., Roentgenology
- 51. Gibe t, Philip D., Camden, N. J., Radiology
- 52. Simere, John H., Chicago, Ill., Radiology
- 53. Sood C. Allen, Rochester, Minn., Radiology
- 54. Frade, Wary Alice, San Francisco, Cal., Roentgenology
- 55. Fray Charles M., Tampa, Fla., Radiology 56. Fram, Homer W., Pittsburgh, Pa., Radiology
- 57. Hall James B., Johnstown, Pa., Roentgenology
- 58. Hantins Walter D., Johnson City, Tenn., Roentgenology
- 59. Hangy, D. Reed, Streator, Ill., Roentgenology
- 60. Harning Walter, Iowa City, Ia., Radiology
- 61. Har well. Wilbur R., Shreveport, La., Radiology
- 62. Hayes, Arthur W., Greenfield, Mass., Diagnostic Roentgenology
- 63. Her mann, Henry C., Louisville, Ky., Therapeutic Radiwingy
- 64. Hierent. Peter E., Kansas City, Kans., Radiology
- 65 Hil Town M., Pittsburgh, Pa., Radiology
- 66 HA Lawrence M., Grand Rapids, Mich., Radiology
- 67 Hoods, Arthur A., Ir., Philadelphia, Pa., Radiology 68 Hootz, Harvey E., Dallas, Tex., Radiology

- 69. Howard, Corbett E., Goldsboro, N. C., Therapeutic Radiology
- 70. Howe, Martha E., New York, N. Y., Therapeutic Radiology
- 71. Hummon, Irvin F., Jr., Oak Park, Il., Roentgenology 72. Hunter, Arthur F., New York, N. Y., Roentgenology
- 73. Jaffrey, George, Olean, N. Y., Radiology
- 74. Jelte, Safford A., Oakland, Cal., Radiology
- 75. Jenkins, I. Warner, Waco, Tex., Radiology
- 76. Jenkins, William F., Columbus, Ga., Roentgenology 77. Jensen, Herman H., Minneapolis, Minn., Radiology
- 78. Jimenez, Juan M. M., New York, N. Y., Radiology 79. Johnson, Roy W., Los Angeles, Cal., Radiology
- 80. Johnston, Wayne A., Dubuque, Ia., Roentgenology
- 81. Kelley, Charles H., Washington, D. €., Radiology
- 82. Kellogg, Douglas S., Ft. Sam Houston, Tex., Roentgenology
- 83. Kestel, John L., Waterloo, Ia., Diagnostic Roentgenology
- 84. Kirsh, Israel E., Salt Lake City, Utah, Radiology 85. Koenig, Edward C., Buffalo, N. Y., Roentgenology
- 86. Lake, William F., Atlanta, Ga., Roensgenology
- 87. Landham, Jackson W., Atlanta, Ga., Roentgenology 88. Larkin, John C., Jr., Berkeley, Cal., Badiology
- 89. Lavine, Sidney B., Trenton, N. J., Diagnostic Roentgenology
- 90. Lavner, Gerald, Haverbill, Mass., Diagnostic Roentgenol-
- 91. Lawlah, John W., Chicago, Ill., Radiology
- 92. LeWald, Leon T., New York, N. Y., Radiology
- 93. Leader, Samuel A., Lexington, Kv., Diagnostic Roentgenologi
- 94. Lerner, Henry H., Boston, Mass., Diagnostic Roentgenol-
- 95. Levy, Abraham H., Brooklyn, N. Y., Radiology
- 96. Lewis, Elbert K., Chicago, Ill., Radiology
- 97. Lia, Bianca Rachel, Boston, Mass., Roentgenology
- 98. Liberson, Frank, Brooklyn, N. Y., Roentgenology
- 99. Logan, George E. C., Philadelphia, Pa., Radiology
- 100. McAlister, Lawrence S., Maskogee, Okla., Radiology
- 101. McCampbell, Herbert H., Knoxville, Tean., Radiology
- 102. McCandless, Oliver H., Kansas City, Mo., Reentgenology
- 103. McCullough, Thomas L., Pittsburgh, Pa., Diagnostic Roentgenology
- 104. McGreer, John T., Dayton, O., Radiologe 105. McKinney, G. C., Lake Charles, La., Roentgenology
- 106. McNattin, Robert F., Chicago, Ill., Therapeutic Radiology
- 107. Mackoy, Frank W., Milwaukee, Wis., Diagnostic Roentgenology
- 108. Magruder, Levin W., New Orleans, La., Radiology
- 109. Manley, Louis V., Northampton, Mass., Diagnostic Roentgenology.
- 110. Martineau, Lawrence A., Providence, R. I., Roentgenology
- 111. Mass, Max, Macon, Ga., Diagnostic Roentgenology
- 112. Maxfield, James R., Jr., Waco, Tex., Radiology 113. Meader, Robert P., Philadelphia, Pa., Rachology
- 114. Mokrohisky, Stephen M., Green Bay, Wis., Roentgenology
- 115. Moore, J. N., Ocala, Fla., Roentgenology
- 116. Morgan, Arthur E., Washington, Pa., Roentgenology Morgan, Harold W., Mason City, Ia., Radiology
- 118. Morris, Clyde L., Peoria, Ill., Roentgenology
- 119. Myers, Karl J., Philippi, West Va., Radiolog
- 120. Nash, Newman C., Wichita, Kans., Radiology
- 121. Neely, John M., Lincoln, Neb., Radiology
- 122. Newton, John O., Cleveland, O., Roentgenology
- 123. Norton, Richard C., Battle Creek, Mich., Diagnostic Roentgenology
- 124. Palmer, James P., Bronx, N. Y., Radiology
- 125. Payne, Andrew K., Jackson, Mich., Radiology
- 126. Pearlstein, Frank, West New York, N. .. Diagnostic Roentgenology
- 127. Pedersen, Nicholas S., San Francisco, Cal, Roentgenology
- 128. Phillips, Allan B., Des Moines, Ia., Radiology
- 129. Piatt, Arnold B., Tulsa, Okla., Roentgenologs
- 130. Plaut, H. F., Mansfield, O., Radiology
- 131. Pollack, Simon, St. Louis. Mo., Roentgenology 132. Popma, Alfred M., Boise, Idaho, Radiology
- 133. Poppel, Maxwell H., New York, N. Y., Roenigenology

- 34. Prince, Norman C., Amarillo, Tex., Roentgenology
- 35. Reed, Harold R., Washington, D. C., Radiology
- 136. Reid, Edward K., Rome, N. Y., Diagnostic Roentgenology
- 137. Rhinehart, B. A., Little Rock, Ark., Roentgenology
- 138. Richardson, Maurice L., Freeport, Ill., Roentgenology 139. Roberto, Romeo, Yonkers, N. Y., Diagnostic Roentgenol-
- 1.0. Roberts, Edward W., Chicago, Ill., Roentgenology
- 1\_1. Robilotti, James G., New York, N. Y., Diagnostic Roentgenology
- 142. Rodes, Charles B., Butte, Mont., Diagnostic Roentgenology
- 143. Rogers, Frank T., Ann Arbor, Mich., Radiology
- 144. Rubin, J. S., Jamaica, N. Y., Diagnostic Roentgenology 145. Sackett, George L., Cleveland, O., Radiology
- 145. Scott, Harry A., Lincoln, Neb., Diagnostic Roentgenology
- 143. Senturia, Hyman R., Chicago, Ill., Radiology
- 142. Sherman, Cyril F., Wichita, Kans., Roentgenology
- 14e. Sickel, Emanuel M., Lakewood, N. J., Diagnostic Roentgenology
- 15C. Silverstone, Sidney M., New York, N. Y., Therapeutic Radiology
- Singer, Bella, Elizabeth, N. J., Diagnostic Roentgenology 141
- Sirca, Dionisie M., Springfield, Ill., Roentgenology
- 153 Sisk, J. Newton, Madison, Wis., Radiology
- 154 Smith, Barney B., Buffalo, N. Y., Roentgenology 155. Smith, Earl D., Utica, N. Y. Radiology
- 156. Smith, Ernest E., New York, N. Y., Radiology
- Sokow, Theodore, Kenosha, Wis., Radiology
- 158. Solomon, Bennet, Springfield, Mass., Diagnostic Roentgenology
- 159. Southworth, J. D., Rutland, Vt., Therapeutic Radiology
- 160. Spencer, Earle W., Saskatoon, Sask., Radiology
- 161. Stacy, Archie J., Tupelo, Miss., Diagnostic Roentgenology
- 162. Sternbergh, W. C. A., Clifton Springs, N. Y., Radiology
- 163. Stewart, Calvin B., Atlanta, Ga., Therapeutic Radiology
- 164. Bzymanski, John J., Passaic, N. J., Radiology
- 165. Talley, Louis F., Marshalltown, Ia., Roentgenology
- Thompson, William G., Holden, Mo., Radiology ruog, Clarence P., Minneapolis, Minn., Roentgenology
- yner, Furman H., Port Arthur, Tex., Radiology
- 169. Vaughn, Robert J., Annapolis, Md., Roentgenology
- 170. Wallace, William S., Durham, N. C., Radiology
- 171. Ward, Leo J., Elizabeth, N. J., Diagnostic Roentgenology 172. Varden, Ralph H., Chicago, Ill., Roentgenology
- 173. Webb, Harold H., Ottumwa, Ia., Radiology
- 174. Wehr, William H., Buffalo, N. Y., Therapeutic Radiology
- 175. Weinstein, Samuel, Brooklyn, N. Y., Roentgenology
- 176. Weitz, Harry L., Traverse City, Mich., Roentgenology
- 177. Williams, Edwin G. C., Danville, Ill., Therapeutic Radiology
- 178. Willis, Augusta Elizabeth, Orangeburg, S. C., Roentgenology
- 179. W Ison, Angus K., Norfolk, Va., Radiology
- 180. Wilson, Russell F., Beloit, Wis., Radiology
- 181. Worth, Harry M., Victoria, B. C., Radiology 182. Wright, Hobart H., Ann Arbor, Mich., Radiology
- 183. Zie inski, John B., Fall River, Mass., Radiology

#### RADIOACTIVE STANDARDS\*

A series of radioactive standards are being prepared under the direction of the Committee on Standards of Radioactivity of the National Research Council. These standards will be deposited at the National Bureau of Standards in Washington, D. C.

<sup>\*</sup> This work is being supported in part by a generous grant from the American Philosophical Society to the Massachusetts Institute of Technology.

to be issued as working standards to investigators who may desire them.

The standards under preparation at present are:

#### (1) Radium Standards

- (a) 100 cc. solutions sealed in 200 cc. Pyrex flasks containing 10<sup>-9</sup> and 10<sup>-11</sup> grams of radium to be used as emanation standards either directly or by subdilution.
- (b) 5 cc. solutions sealed in Pyrex ampoules containing 0.1, 0.2, 0.5, 1.0, 2.0, 5.0, 10, 20, 50 and 100 micrograms of radium to be used as gamma-ray standards. If desired, these may be obtained in sets of 13 with two each of the 0.2, 2, and 20 microgram standards.

#### (2) Thorium Standards

Sealed ampoules containing sublimed ThCl<sub>4</sub>. These may be used in preparing standard thorium solutions.

Directions for use will be furnished with the standards.

#### (3) Standard Rock Samples

The following rocks, ground to pass 40-mesh screen and be retained on 100-mesh screen are available in 100 gram samples.

Quartzite (Virginia)

Triassic diabase (Virginia)
Milford granite (Massachusetts)

Chelmsford granite (Massachusetts)

Gabbro-diorite (Massachu-

Columbia River Basalt (Idaho) Bearea sandstone (Ohio) Dunite (North Carolina)

Carthage granite (Missouri)
Carthage limestone (Missouri)
Deccan Trap (India)

Kimberlite (South Africa)

These samples of rock will be analyzed for radium and thorium content and are intended for use as working standards to

check methods used in extraction of radon and thoron from rock samples. They may be used for direct fusion in the electric furnace or for carbonate fusion.

All of the above samples will be analyzed at a number of laboratories equipped to make such measurements and ultimately certificates will be issued by the National Burrau of Standards. This work is in progress but will require considerable time for its completion so that final figures are available only for a part of the samples at the present time.

Accurate knowledge of the radioactive content of the materials of the earth's crust is of primary importance in many phases of geology, geophysics and cosmology. Reliable radioactive standards are also essential in stadies of radium and thorium poisoning and in biological and medical investigations using the technique of radioactive indicators, or internal artificial radioactivity therapy. For the latter purposes calibrated standard sources of  $\beta$ -rays will be made available.

It is boped that the standards which have been prepared by the Committee will provide all workers in these fields with a common basis for comparison of measurements and also improve the accuracy of all measurements of this type. It is likely that they will have other applications and the Committee would appreciate hearing from interested persons who may desire similar standards for their work. The Committee is also glad to cooperate as far as possible in aiding investigators to use these standards to the best advantage and welcomes specific inquiries regarding their use. It is urged that any suggestions regarding other desirable radioactive standards, not at present available, be submitted promptly to the Committee. In particular, it will facilitate the work of the Committee if those laboratories and individuals which can make use of these standards advise the Committee of their probable requirements.

Communications may be addressed to the Charman, Professor Robley D. Evans, Department of Physics, Massachusetts Institute of Technology, Cambridge, Massachusetts.

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## CLINICAL CONFERENCE OF MID-WESTERN RADIOLOGISTS

The Fourth Annual Clinical Conference of Mid-Western Radiologists was held at the Brown Hotel, Louisville, Kentucky, on February 9 and 10, 1940. Presentations on many subjects of interest to radiologists were made by some of the leading physicians of Kentucky.

At the dinner meeting Dr. William Allen Pusey, of Ch cago, Illinois, spoke on the subject "Reminiscences of my Early Experiences with the Roentgen Ray." He presented his office record and case history of the first patient he had ever treated with the roentgen ray, this being done early in the year 1900. He spoke of his therapeutic experiences with the roentgen ray in lesions

of many types, many of which were undoubtedly so treated for the first time.

Dr Irvin Abell, of Louisville, Kentucky, then spoke on the subject "The Present United States Public Health Program." In prefacing his major presentation he paid a glowing tribute to the radiologist. He sooke of his great importance in the general field of medicine and of the many contributions to medical progress that had been made by radiologists during the last forty years. He also commended radiologists in general for the work that they were doing in preserving their specialty and for their defense against the attempted inroads of so-called Social Legislation. He then gave a remarkable summary of the legis ative activities of our Government in the field of medicine during the past six years, together with a summary of the legislat on now before the Congress.

Dr. C. A. Good, of the Mayo Clinic, in behalf of Dr. B. R. Kirklin, invited the Conference to meet in Rochester, Minnesota, next year. The invitation was accepted by the Conference.

I. C. Bell



#### BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review at the interests of our readers as space permits.

Chronic Diseases of the Abdomen: A Diagnostic System. By C. Jennings Marshall, M.S., M.D. (Lond.), F.R.C.S. (Eng.), Surgeon, Charing Cross Hospital and Victoria Hospital for Children; Surgical Consultant, L.C.C., and Bromley District Hospital; Examiner in Surgery, London University and Victoria University, Manchester. Cloth. Price, \$6.00. Pp. 247, with 131 illustrations. Boston: Little, Brown & Co., 1939.

As the author states in the preface, this volume is an endeavor to present in concise form for the use of the general practitioner the chronic conditions which affect the abdomen.

In Part I, he emphasizes that the abdomen cannot be considered apart from the rest of the body and in the notes on the history taking and physical examination it is pointed out that one must always think of the patient as a whole. His suggested physical examination is complete, although his avowed aim is determining abdominal troubles. A section on Special Investigations includes roentgenography, instrumental examinations such as proctoscopy, cystoscopy, gastroscopy, etc., and laboratory examinations such as urine, feces, blood, renal function tests, etc.

Part II deals with differential diagnosis and here the author takes up pain, and its significance, as it may arise from various abdominal systems and organs or is made manifest as referred from other anatomic sites such as the spine or chest. Intra- and extraperiteneal conditions are discussed and differentiated, and backache is taken up in detail. Finally, there is a section on "Other Symptoms" which covers hematemesis, jaundice, loss of weight, diarrhea, hematuria and vomiting.

The author has shown excellent balance throughout and always gives due emphasis to various symptoms. The limitations of different procedures are recognized and this is nowhere more evident than in the section on roent-genography which is perforce very abbreviated. Roentgenograms "are indispensable in many cases, in others of great help, but wherever they are employed merely as a short cut to assoid thinking, they are a menace."

Appropriate diagrams and roentgenograms illustrate the book. Nowhere does one get the impression of "padding." For the roentgenologist who wishes a good yet brief treatise on the "chronic al-domen," this book can be recommended.

H. D. KERR

MALADIE DE RECKLING-HAUDEN, MALADIE DE PAGET, LIPOIDOSES OSSEUSES, MYELOMES MULTIPLES. Par Dr. I. Snapper, Professeur à l'Université d'Amsterdant. Traduction du Professeur dr. F. de Wit e (Fand) et le dr. G. Coryn (Bruxelles). Cloth. Price, 330 fr. Pp. 192, with 22 plates. Paris: Masson et Cie, 1938.

In tais clume, chronic cystic osteitis or von Recklinghausen's disease of bone, osteitis deformans or Paget's disease, xanthomatosis, Gaucher's disease and multiple myeloma are described of detail. Almost one-half (84 pages), is deveted to von Recklinghausen's disease.

In the first chapter, a review of the literature of chrenic eystic osteitis is followed by a discussion of the relationship between it and the patholeg cal changes found in the parathyroid glands, a description of the microscopical changes found in hyperplasia and adenoma of the parathyrcids and a review of the criteria on which to base a differential diagnosis of these pathelogical changes. The roentgenological characteristics, the pathological variations in calcium and phosphorus metabolism and the mecroscopical skeletal changes are described ir ample fashion. Case reports of patients who were operated upon by Snapper for removal of adenomata of the parathyroids are incused. In these patients, recalcification of the keletor occurred after operation. In the second and third chapters, the question of hypert opay of the parathyroids caused by primary Assurbances of calcium metabolism, and the effect of removal of normal parathyroics in ankylosing arthritis, scleroderma and other diseases are discussed.

The description of Paget's disease is covered in a chapter of 30 pages. While the symptomatorogy, etiology, biochemical changes,

roentgenographic characteristics and other features are fully described, the omission of any reference to osteoporosis circumscripta is worthy of mention. The remaining chapters are devoted to xanthomatosis, Gaucher's disease and multiple myeloma. Throughout emphasis is placed on the differential diagnosis of these various conditions and von Recklinghausen's disease.

The book is illustrated with 22 plates reproducing roentgenograms, microscopical and gross specimens and clinical photographs of the diseases described. The illustrations are clear and are excellent from every point of view. The bibliography following the chapters on von Recklinghausen's disease is voluminous but the number of references for the other diseases is, in comparison, small. However as the volume is actually a monograph on chronic cystic osteitis and its differential diagnosis, this is not a serious defect. It can be recommended as a concise reference book for these interested in the diagnosis and treatment of these diseases of bones.

R. S. Bromer

END-RESULTS IN THE TREATMENT OF GASTRIC CANCER: AN ANALYTICAL STUDY AND STA-TISTICAL SURVEY OF SIXTY YEARS OF SURGI-CAL TREATMENT. By Edward M. Livingston, B.Sc., M.D., Associate Visiting Surgeon, Bellevue Hospital, New York; Assistant Clinical Professor of Surgery, New York University College of Medicine, and George T. Pack, B.Sc., M.D., F.A.C.S., Attending Surgeon, Memorial Hospital, New York City; Assistant Professor of Clinical Surgery, The School of Medicine, Yale University, New Haven and Cornell University Medical College, New York City. With a Foreword by Bowman C. Crowell, M.D., Associate Director, American College of Surgeons. Cloth. Price, \$3.00. Pp. 179, with numerous charts. New York: Paul B. Hoeber, Inc., 1939.

This small volume, prepared as a single chapter in a comprehensive treatise on the treatment of cancer and allied diseases soon to be published, contains a careful analysis of the results produced by surgery in cancer of the stomach, beginning with the first successful resection performed by Billroth almost sixty years ago. Although one-third to one-fourth of all cancers occur in the stomach, the absolute

curability of the disease at the present time amounts to less than 5 per cent. An attempt is made to offset this depressing figure by repeatedly emphasizing the observation that of the 30,000 to 50,000 cases developing in the United States each year, approximately 10,000 are resectable. Since this incidence equals that of cancer of the breast, and is much higher than that of many other forms of cancer, the authors believe that resectable cancer of the stomach should be considered as a separate entity in which the prognosis is no worse than it is in mary other forms of malignant disease. From a stady of 14,000 operations collected from the better surgical clinics of the world, and tabulated in the back of the book the conclusion is reached that good surgery carried out by properly trained teams should permanently cure at least 20 per cent of the resectable group. Such reasoning will serve as a stimulus to those who undertake radical operative procedures. but it offers little solace to the 28,000 to 48,000 patients who obtain little relief and die each year.

An elaborate supplement contains thirty charts and tables beautifully prepared as a graphic presentation of the points made in the text. Because of the technical excellence of this material lantern slides can easily be prepared from it for teaching purposes. The bibliography includes 358 references and is very complete. In another supplement, a study of statistics for this country, compiled over a fifteen year period, shows 244,357 deaths from war, 441,912 fatalities from traffic injuries, and an estimated death rate of 600,000 from cancer of the stornach. These figures are graphically depicted in poster form on the fly-leaves at the front and back of the book.

CHARLES L. MARTIN

THE CONSTRUCTION OF VULCANITE APPLICATORS FOR APPLYING RADIUM TO LESIONS OF THE BUCCAL CAVITY, LIPS, ORBIT AND ANTRUM. By Desmond Greer Walker, M.A., M. Dent. Sc., M.B., B.Ch., Assistant Dental Surgeon to the Royal Dental Hospital; Dental Registrar at the Middlesex Hospital; Chief Assistant to the Plastic Department, St. Bartholomew's Hospital. Foreword by W. Warwick James, O.B.E., F.R.C.S., L.D.S. Cloth. Price, 5/- Pp. 61, with 23 plates. London: John Murray, 1938.

This small sixty-one page book is prepared

by a dentist for the guidance of others in his profession who may be called upon to prepare surface radium applicators for the treatment of malignant tumors in the mouth and cavities of the bones of the face. The principle of using multiple small, heavily filtered radium sources fixed a short distance from the tumer surface is advocated and the applicators are carefully made so that they may be worn with comfort over considerable periods of time. The distance factor is provided by a thin layer of Columbia paste placed in a protective shield of lead and covered by a carefully fitted vulcanite shell made to accurately conform to the part treated. When the completed device is assembled it is, in many instances, held in place by bars attached by springs or straps to a head band. Numerous photographs included in a series of 23 plates illustrate the method adequardy, and careful directions are given for the preparation of the materials used. For those who elect to utilize this elaborate form of radium therapy which has much to commend it, especially in the care of superficial lesions overlying bony surfaces, the book should prove most valuable. CHARLES L. MARTIN

SOBRE A RADIOLOGIA DO CANAL OPTEO. By H. C. P. Marback, Bahia, Brazil. Pp. 89, with 45 plates. Bahia: Imprensa Regina, 1939.

This monograph, written as a competitive thesis, reviews the embryologic development, anatomic structure and anthropomorphic determination of the positions of the optic canals. It mentions and comments on the various techniques (some 30 in all) employed for making roentgenograms of these structures.

The author then presents his own improved technique and recommends it for general use.

In this method a cage-like device is attached to the recent gen tube to fit over the patient's head and hold a small film perpendicular to the mimar pencil of rays. In operation the patient is seated with the head steadied on a chin support, with the Virchow plane (plane of Reid's line) corresponding to the horizontal plane. The device is placed over the head, and the rule "must be moved in such manner as to annual angles alpha and beta" of the optic canals. These angles are achieved by directing the title downward for the angle alpha (25 degrees mean) and obliquely for the angle beta (Todesees). With the tube set at these angles the device must be lined up with the patient's head, so that the primary rays strike the skull at Jammann's point, to pass through the canal and erserge at Brunetti's point (center of the lower and outer quadrant of the orbit) to expose the film.

Marrick's technique is not adaptable to routine practice and does not fill the requirements for a practical method. Too much is left to the judgment of the technician. A number of exposures are recommended by Marback for each canal. Thus true contours apparently are not consistently obtained. The method makes the projection of the canals a special procedure, several pieces of special apparatus being mequired. It does not allow for symmetrical projection of the canals, a requirement which is essential for their comparison, for it is not emough to examine only one canal in any given case. Stereoscopic projections can scarcely be made with the technique.

RAYMOND L. PFEIFFER



#### DEPARTMENT OF TECHNIQUE

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### SIMPLE METHOD FOR ROENTGENOGRAPHY OF THE OPTIC CANAL

By M. MORRIS WITTENBERG

THE optic foramina can be perfectly demonstrated by the use of the Bullitt mastoid apparatus.

at the crosslines and the head is immobilized in the manner provided by the apparatus (Fig. 2). The patient may be studied in

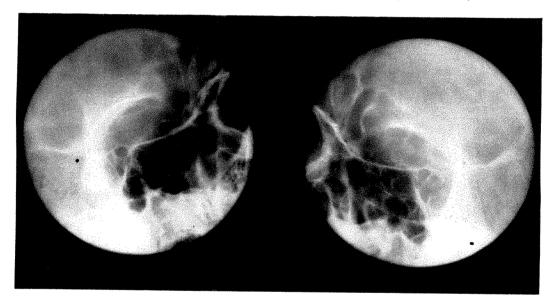


Fig. 1. Roentgenogram showing both canals and some of the accessory sinuses.

With this apparatus identical comparative studies can be made of both sides and duplicated at any future date (Fig. 1). The procedure is simplified considerably since the orbit to be examined is constantly visible throughout the study and the head is perfectly immobilized. There is no necessity for measuring devices or for focusing the tube. This mastoid apparatus is already in use in most hospitals and private offices so that no additional apparatus is necessary.

The patient is placed in the supine position with the head rotated oblique. To so that the corresponding orbit touches the cellulose sheet. The center of the orbit is placed

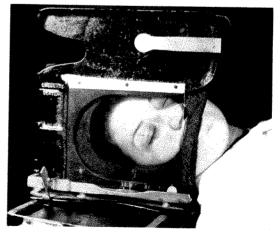


Fig. 2. Apparatus with patient in position. Notice the relationship of the orbit to the crosslines.

prone position with equally satisfactory results and stereoscopic studies may be obtained by utilizing the shift. The posterior ethmoidal and sphenoidal sinuses are visualized as with the Rhese position and again permits an exact comparison and duplication of both sides.

The exposure necessary and the masking device used are the same as with mastoid studies (Fig. 3) except when the examination is made in the prone position. The sides are then reversed and a special blocking out mask is necessary.

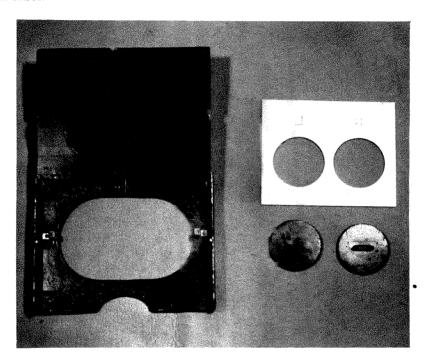


Fig. 3. Bullitt massing device and the one used when employing the prone position.



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# ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

#### ROENTGEN DIAGNOSIS

HEAD

Jones, William A. Further observations regarding familial multilocular cystic disease of the jaws. *Brit. J. Radiol.*, April, 1938, 11, 227-240.

Author's Summary: Further observations regarding a peculiar condition occurring in three members of the same family are given. These cases were first described by the author at the meeting of the Radiological Society of North America at St. Louis, Dec. 1, 1931, and published in the American Journal of Cancer, April, 1933. The condition is one of multiple dentigerous cysts occurring universally throughout both the upper and lower jaws, and accompanied by a chronic hyperplastic disorder of the cervical lymph glands of the submaxillary regions.

The condition presents itself toward the end of the second year of life and is accompanied by bilateral painless swelling of both upper and lower jaws.

Roentgenograms and photographs of these children made in 1931, and again in 1937, are shown, and the course of the disease is discussed. A fourth member of the family has escaped and presents normal dental development. A fifth member of the family (sixteen months old) already presents a suspicious bulge at the angle of the left side of the lower jaw. There is no evidence of a like condition in a previous generation of either side of the tamily.

Through the kindness of Dr. P. J. Thomas, of Savannah, Ga., the author has at his disposal the description, with roentgenegrams and photographs, of a similar case in a boynow eleven years of age. In this case the multi-locular cysts of both jaws are also observed. There is, however, in this patient, no evidence of lymphatic glandular involvement. Dr. Thomas has produced a genetic chart showing the descent of the anomaly through five generations of the family of this patient.—S. G. Henderson.

BLADY, JOHN V., and HOCKER, ALFRED F. Sialography, its technique and application

in the roentgen study of neoplasms of the paround gland. Surg., Gynec. & Obst., Dec., 1938, 67, 777-787.

The sechnique, indications and contraindications of sintegraphy are discussed. Inasmuch as no larraful effects from its use have been noted, t appears that its use should be more generally accepted. The authors have found it of value a the determination of the relationship of the normal fuct system and gland tissue to adjacent structures, for the demonstration of salivary fistulae, duct stones, foreign bodies or strictures, in diagnosing chronic recurring inflamration, and to determine the nature of a grow has to whether it is encapsulated, infiltratire or is a mass extrinsic to the gland and ducts proper. The irregular filling defects in the gland serveture and the filling defects in the finer remircations of the duct system produced by an infiltrating tumor are quite characterstic. The knowledge gained from the sialogram will help determine the operative plan more accurately prior to operation and herein is sts greatest value.—P. C. Swenson.

Swinten, Neil W., and Warren, Shields. Salivery gland tumors. Surg., Gynec. & Obst., Oct., 1968, 67, 424-435.

Eighty-one tumors of the salivary glands are reported. The concepts of origin of these tumors are thoroughly discussed. The authors favor the concept that the tumors arise from misplacement of cells during the rather complex embryomic development of the face. They present 51 mixed tumors with clinical data. Their variable histological picture is stressed, as well as some of the less common benign tumors Of the mixed tumors operated upon at the Laber Cinic 4.3 per cent recurred. Careful complete excision of the salivary gland tumor withou rupture of the capsule or spilling of its contents must be done if recurrence is to be prevensed. This may involve sacrificing the facial Eerve. Although the results of radiotherapy have not been encouraging, the authors feel that with further experience the results may be improved. Combined radical excision and raletherapy should be continued in all malignant sumors until it is definitely proved

that radiotherapy is of no value. Three of 9 malignant tumor cases are alive and well two and four years after operation. The diagnosis of malignancy is based on the finding of combined cellular anaplasia or metaplasia, invasive properties, and evidence of rapid growth in whatever tissue these changes might make their appearance. Invasive growth alone, although ordinarily a helpful diagnostic point in the case of malignant tumors, is valueless in the group of salivary gland tumors.—P. C. Swenson.

#### NECK AND CHEST

RAY, Bronson S., Tumors at the apex of the chest. Surg., Gynec. & Obst., Nov., 1938, 67, 577-599.

Five cases of apex tumors are added to the literature, all of different histologic structure but of similar clinical manifestations as in the cases described originally by Pancoast and others. The literature is reviewed. The neurological aspects of the cases are emphasized, particularly the surface pain and its segmental distribution, the sensory changes, sympathetic irritation, cord compression, etc. There is very little if any help from roentgen or radium therapy. Treatment must be directed toward the surgical relief of pain wherever possible, and this makes early diagnosis important.—

P. C. Swenson.

FRIEDMAN, TOWNSEND B., and MOLONY, CLEMENT J. Rôle of allergy in atelectasis in children. Am. J. Dis. Child., August, 1939, 58, 237-249.

The authors report 6 cases of nontraumatic, nonpostoperative atelectasis and I case of postoperative atelectasis occurring in allergic children. They conclude that the processes in
bronchial asthma which may produce bronchial
occlusion are bronchospasm, thickening of the
bronchial walls, secretion of thick mucus and
paradoxic collapse of the bronchi during expiration. All evidence seems to point to
bronchial occlusion as the principal cause of
atelectasis. They suggest the possibility of recurrent atelectasis as a precursor of bronchiectasis.

The paper is profusely illustrated with reproductions of the roentgenographic changes in the lungs in the cases of their series. They regard the treatment as twofold. One is concerned first with the immediate relief of the patient and second with methods of preventing recurrence. Treatment is directed at removing the mucous plug from the bronchus. The orcinary indirect methods are postural drainage and the use of expectorants and drugs which increase the bronchial secretion or render it more liquid. Epinephrine hydrochloride given subcutaneously, while it makes the patient more comfortable, does not serve to release the tenacious, thick mucoid plugs. If the condition persists, they believe that immediate bronchoscopic aspiration is the method of choice, and the aspiration may have to be repeated until the pulmonary tree is free of obstruction.

In order to prevent recurrence a thorough allergic study of the cause of the asthmatic attacks should be made and by preventing the seizures, recurrences of the atelectasis should be eliminated.—R. S. Bromer.

KAUTZKY, A. Grenzen bronchographischer Diagnostik der beginnenden Bronchiektasienbildung. (Limits of bronchographic diagnosis in early bronchiectasis.) Fortschr. a. d. Geb. d. Röntgenstrahlen, Feb., 1938, 57, 168–176.

The fully developed case of bronchiectasis with definite dilatation of the bronchi offers no difficulty in diagnosis. The border line cases are difficult. The bronchi normally become narrower as one approaches the periphery. When this progressive narrowing stops, a dilatation is present. Occasionally, however, there is widening of a bronchus without a true ectasia being present, and, on the other hand, differences sometimes occur between the bronchographic and the autopsy findings. The indirect signs of bronchiectasis are a failure of the alveoli to fill with lipiodol, a tortuosity of the bronchi, and third a failure of the lipiodol to show a peripheral motion during inspiration. This latter sign occurs in all parenchymal diseases and indicates a defective areation of that portion of the lung. These three signs may be present before a definite ectasia is demonstrable and may lead to an earlier diagnosis. Repeated observations over a long period are dezirable.—W. A. Evans, Fr.

BCYD, LINN J., and McGAVACK, THOMAS H. Aneurysm of the pulmonary artery. Am. Heart J., Nov., 1939, 18, 572-578.

Aneurysm of the pulmonary artery is rare. About 139 cases had been reported up to 1936. By definition the term is limited to those

dilatations which are the result of, or associated with, actual damage to one or more coats of the vessel. The sex distribution is about equal and the mean age 37.7 years with 34 per cent of the cases under thirty years of age. The trunk of the artery is most commonly affected and the saccular dilatation is a little more common than the fusiform type. Right and left branches are involved equally often. In the etiology, trauma seemed to be a factor in 3 cases, congenital anomalies were significant in about one-half, and arteriosclerosis was regarded as a provocative in 23 per cent. Syphilis was regarded as responsible for all cases by Warthin, but the figure is rare, probably per cent and that may be too high. In a few sases, septic or rheumatic endocarditis appeared of etiologic importance.

The common symptoms are dyspnea, cyanosis, pain, palpitation and cough. On physical examination there is enlargement of the mediastinum toward the left at the second and third costal cartilages and in 2 cases there was erosion and necrosis of these cartilages. A harsh systolic murmur is usually heard in this area. Right-sided cardiac enlargement is almost constantly present at autopsy, but is often missed during life.

Roentgenologically there is observed to be a prominence in the region of the pulmarary conus which pulsates if a thrombus is not present and gives a "seesaw" movement to the left side of the silhouette. In the right anterior oblique view there is encroachment on the retrosternal space and there may be a knob-like projection into the posterior mediastimum beneath the aortic arch.

In the differential diagnosis, aortic aneurysm, patency of the ductus arteriosus, diopathic dilatation of the pulmonary artery, and various congenital malformations must be considered.

The authors report 2 cases, one a syph litic Portuguese, aged forty-two, with an aneurysm localized in the left main branch of the pulmonary artery by the method of Robb and Steinberg, and also at operation performed under the mistaken diagnosis of carcinaria of the lung. The second case was a male syph litic, aged sixty-one, who exhibited roentgenosiopically a dilatation of the pulmonary comes and a superimposed semilunar shadow the size of a peach. In both cases the aneurysms were regarded as syphilitic in character.—W. A. Evans, Fr.

TESCHENDORE, WERNER. Röntgenologische Herzfurktionsprüfung. (Roentgenologic tests of card at function.) Fortschr. a. d. Geb. d. Röngensmählen, Sept., 1939, 60, 214–235.

There are four roentgen methods of testing circulatory function: (1) kymographic studies of the heart before and after exercise; (2) the method of the Abreu involving the correlation of changes in the surface area of the heart with cardial volume and body weight; (3) measurements of the cardiac volume before and after exercise; (4) the Valsalva test.

In regard to the first method, the normal heart exhibits a diminution in size following exertion with an increase in the amplitude of the pulsation. In cardiac insufficiency there is an increase in the size of the heart and a diminution in amplitude following over-exertion. Care must be taken that the exposures are made in the same phase of respiration to insure a constant position of the diaphragm leaves

The method of de Abreu is concerned with the relation of the volume change in the cardiac cycle measured kymographically to the cardiac volume and the body weight. For these measurements the author has used an egg-shaped vector kymograph and the values are introduced into the formula e.v.=D.P.t. where e is the systelic retraction of the cardiac border, v the heart volume, D the pulse volume, P the blood pressure and t the work time. In the formula e.v./P where P is the body weight the value should be about 4 for men and 3.6 for women.

The heart volume is best measured by the method of Lysholm with simultaneous postero-anterior and lateral exposures and application of the Rehver-Kahlstorf formula. Measurements before and after exercise show a diminution of volume in the normal heart while there is an increased volume in the heart of impaired efficiency.

The author highly recommends the quantitative Valentva test carried out by the method of Bürger before and after exertion. Some modifications are necessary for gravely ill patients and the contraindications are aortic and parline aneurysm, advanced coronary arter disease, heart block, and severe cardiac insufficiency. The normal heart decreases in size on posts sides during the test. After exercise the cecrease is less marked on one or both sides. The left side does not partake of the

decreased size in hypertrophy of the left ventricle. The failure of the right side to diminish is uncommon and usually accompanies congestion of the lesser circulation. If the heart does not decrease in size at all it is a sign of severe insufficiency and carries a poor prognosis. A fifth possibility is that there is a greater dimunition in size after exercise and this occurs with flabby atonic hearts and a poor prognosis.-W. A. Evans, Fr.

Ash, Rachel, Wolman, Irving J., and Bromer, R. S. Diagnosis of congenital cardiac defects in infancy, Am. 7. Dis. Child., July, 1939, 58, 8-28.

This report consists of an analysis of 32 cases of cardiac anomalies which were verified at autopsy. Of the 32 cases, a correct diagnosis was made or suggested in only 14. An attempt is made to evaluate the diagnostic features associated with congenital heart lesions in infants. The following symptoms and physical signs are discussed in detail: cyanosis, polycythemia, thrills, murmurs. There is also a discussion of the electrocardiographic and roentgen findings. The authors comment on the clinical features of the more usual cardiac defects, interventricular septal defect, interatrial septal defect, patency of the ductus arteriosus, pulmonic stenosis, the tetralogy of Fallot, complete transposition of the great vessels, defective development of the right ventricle associated with atresia or hypoplasia of the tricuspid valve, and anomalies of the coronary vessels.

The roentgenologist can determine whether the individual chambers of the heart are large or small and whether abnormal pulsations or other vascular changes are in evidence, but he should not be expected to indentify intracardiac lesions. As a result of the increase in the cardiac shadow to the right of the sternum in the anteroposterior view, an enlarged right atrium gives rise to the appearance of a globular heart situated in the midposition. In the noncyanotic infant the most frequent cause of such a globular heart is a defect of the interatrial septum, usually persistent patency of the foramen ovale. Enlargement of the conus of the right ventricle is always associated with some degree of fullness in the left median or pulmonic arc. Marked enlargement of the cardiac contour to the left not infrequently is due solely to hypertrophy of the right ventricle. This can

be verified by noting anterior bulging of the cardiac shadow in the lateral or the oblique view, with no posterior cardiac enlargement. The position of the left apex fails to differentiate between enlargement of the left and enlargement of the right ventricle. Aneurysmal enlargement of the pulmonary artery from any cause reveals itself as a rounded prominence in the pulmonic region. In the authors' series it was associated with (a) patency of the ductus arteriosus, (b) stenosis of the pulmonic valve and (c) dilatation of the pulmonic valve, interventricular septal defect and dextroposition of the aorta (Eisenmenger's complex).

The pulmonary artery distal to a malformed, contracted valvular ring is often dilated and appears in the roentgenogram as an enlarged pulmonary arc. But if, as happens more frequently, there occurs developmental hypoplasia of the infundibular region of the right ventricle and pulmonary artery, concavity or sharp angulation in the region of the pulmonic arc will be seen.

Atrophy of the left ventricle may manifest itself in lateral and oblique views as a flattening of the posterior outline of the heart with increase in the clear space between the heart and the chest wall. If the right ventricle is of normal size, hypertrophy of the left ventricle should be associated with diminution of the clear space posterior to the heart. However, if the heart consists largely of an enormous left ventricle, the right ventricle being merely a small appendage, the left may then be displaced anteriorly and no encroachment on the posterior clear space is shown but rather a seeming anterior enlargement simulating hypertrophy of the right ventricle.

Either pulmonary or aortic atresia and transposition of the great vessels may present a narrowed mediastinal shadow on roentgenoscopic examination. In the oblique position, this shadow should remain unchanged in the presence of atresia of either of the great vessels but should broaden out in the presence of transposed vessels.

A narrow mediastinal shadow associated with transposed vessels in the anteroposterior roentgenogram occurred in only 25 per cent of the cases of the series reported. More frequently the tremendously enlarged right auricular appendage projecting upward into the mediastinum caused a widening of the mediastinal shadow on the right side. When in

association with transposition of the great vessels the left ventricle became hypertmophied, there seemed to be a special tendency toward dilation of the right atrium and auricula.

In interventricular septal defect, the roentgen contour is unchanged, or some degree of hypertrophy of both the right and left ventricle may be noted in the lateral and oblique view. Interatrial septal defect is shown in the anteroposterior view as definite enlargement to the right of the sternum due to enlargement of the right atrium. The characteristic outline is globular. The hilar shadows are increased. Hypertrophy of the right ventricle may be noted in lateral and oblique views. If in a noncyanotic infant presenting a murmur of the type associated with an interventricular septal defect, the heart shows definite enlargement of the right atrium together with marked enlargement of the right and perhaps also of the left ventricle as observed in lateral and oblique views, there probably exists both an interventricular septal defect and an interatrial defect.

In patency of the ductus arteriosus, the roentgenogram shows most frequently enlargement of the right ventricle, with some prominence of the pulmonic arc and increased hilar shadows. Under the roentgenoscope increased pulsations are visible in the pulmonary artery and the hilar regions.

In pulmonic stenosis the roentgenescopic examination should show the hilar densities as small in comparison with the prominent pulsating shadows typically associated with patency of the ductus arteriosus.

In the tetralogy of Fallot, the roemgen appearance varies with the site of the lesion. If there exists the customary developmental hypoplasia of the conus of the right ventricle and of the pulmonary artery, a concavity or a sharp angulation may be present in the region of the pulmonic arc. On the other hand, stenosis of the cusps with dilatation of the vessel beyond the site of the stenosis may be associated with an enlarged pulmonic arc. In addition the mediastinal shadow is usually enlarged to the right, and lateral and oblique views will demonstrate hypertrophy of the right ventricle. Not infrequently hypertrophy of the right ventricle is so pronounced that the lower pole of the cardiac apex is formed by the right ventricle, the left ventricle being displaced upward. In such cases the apex of the cardiac shadow may have a blunt, straight appearance

which has been likened to the tip of a wooden shoe (commer en sabot).

In transposition of the great vessels, the roer tgenescopic examination may be narrow in the anzeroposterior view but should broaden out in the lateral and oblique views.

In defective development of the right ventricle associated with atresia or hypoplasia of the tricuspid valve, the diminutive size of the right ventricle is seen in the roentgenogram (a) in the anteroposterior view, as a concavity in the region of the pulmonic conus, and (b) in the left anterior oblique view, as absence of carciac shadows anterior to the shadow of the aorta.—R. M. Harvey.

GIEFING, JOHN F., and CHARR, R. The hear in anthracosilicosis. J. Am. M. Ass., Aug. 22, 1939, 113, 574-576.

Consistive heart failure is a common occurrence in cases of far advanced anthracosilicoss. In a series of postmortem examinations made anthracite miners, heart disease was found to be twice as common in the miners as in normaners. In the present study only the mirers without clinical evidences of congestive heart radure were studied. Twenty-five miners were studied. The ages of the miners varied from thaty-six to sixty-seven. The duration of ther occupation varied from three to forty years. All the miners had either moderately or far ad-anced anthracosilicosis, as evidenced by eitker nodular or massive consolidation in the lunes revealed by roentgenographic examinations. Nine, in addition to anthracosilicosis, hae either moderately or far advanced pulmorary tuberculosis.

The blood counts showed secondary polycytheria in most instances. The vital capacity was refreed in all cases in direct proportion to the execut of the anthracosilicosis. The venous presure in most cases was within the normal lings. The velocity of the pulmonary and of the complete circulation was practically normal in all the rases. Roentgenographic examination of the heart showed no enlargement except in 2 cases. The aortic knob was prominent in most cases. The functional tests showed that practical v all the miners studied had abnormal accele action of the pulse rate after slight exertion. The electrocardiograms in the majority of instances showed myocardial damage.— S. G. Anderson.

#### ABDOMEN

RIVERS, ANDREW B. The importance of cancer as a cause of chronic dyspepsia. J. Am. M. Ass., Sept. 23, 1939, 113, 1188-1192.

The object of the study reported in this paper was to gather some information relative to the frequency with which cancer is found to be the cause of indigestion. The organ most frequently invaded by cancer responsible for dyspepsia was the stomach. Next in order of frequency was the pancreas. Carcinoma of the pancreas is much more frequently found in men than in women. This is true also of carcinoma of the esophagus. The author concludes that:

- 1. Dyspepsia is caused by cancer much more frequently in men than in women.
- 2. Cancer begins to become a relatively frequent cause of indigestion in both sexes at about the age of forty-five.
- 3. There is a pronounced increase in the incidence of cancer as the cause of indigestion in later life. In this series, of the men beyond the age of seventy years who had a primary complaint of indigestion 58 per cent were found to have malignant disease.
- 4. Men seem to progress into a definite dyspepsia-cancer age from five to ten years earlier in life than women. This age in men started in the late fifties and in women between the ages of sixty-five and seventy years.
- 5. After the age of forty-five symptoms of dyspepsia should be evaluated with meticulous care and this should include roentgenologic investigation.
- 6. An educational program having for its purpose the enlightenment of the public with regard to the hazards of nonprofessional treatment of dyspepsia after the age of forty-five, and particularly throughout the dyspeptic-cancer age period would produce some highly desirable results.—S. G. Henderson.

CARTER, R. FRANKLIN, and COLLINS, HAROLD L. Anomalies of the bile ducts; report of two cases with operations and autopsies. Am. J. Dis. Child., July, 1939, 58, 150-161.

The authors report 2 cases of anomalies of the biliary tract. In one there was cystic dilatation of the extrahepatic ducts with an unusual arrangement and number of ducts; in the other, stenosis at the papilla of Vater.

The symptoms of cystic dilatation of the bile ducts are variable, and the condition is seldom diagnosed preoperatively. The condition is usual y found in a person about eighteen years of age who has had symptoms referable to the biliary tract, such as nausea, pain and intermittent attacks of jaundice. At times a tumor may be palpated in the right upper quadrant of the abdomen. The clinical picture of congenital atresia is that of complete obstruction of the biliary passages. Jaundice may be present at birth, but more often the child appears normal, becoming jaundiced three or four days later. This jaundice usually increases to the point where at three to four months the infant has a grayish-green color. The liver increases in size but the nutrition remains good. The condition must be differentiated from icterus neonatorum, syphilitic hepatitis, congenital hemolytic icterus, jaundice of sepsis and jaundice cue to enlarged lymph nodes. When the diagnosis of cystic dilatation or atresia of the ducts has been made, an exploratory laparotomy is indicated.—R. S. Bromer.

Meves, F. Röntgenbefunde bei der chronischen Amöbenruhr. (Roentgen findings in chronic amebic dysentery.) Fortschr. a. d. Geb d. Röntgenstrahlen, August, 1939, 60, 175–180.

These studies were carried out at Tübingen from 1935 to 1937 by means of barium enema with films before and after expulsion of the barium and also with the air contrast study of the colon. All patients were carefully studied clinically, bacteriologically, and rectoscopically. A segmental colitis is common in chronic amebic dysentery. The affected parts of the colon appear atonic with an absence of the normal haustrations and with very fine tooth ine serrations of the wall. They are very sensitive to palpation. After evacuation the ulcerations of the mucosa may be seen. Deep penet-ating ulcers were encountered very rarely in this group of cases. Where the bowel was very atonic the mucosal relief pattern was not obtained. As a rule films exposed immediately after defecation show emptying only of the sigmcid and rectum except in severe cases with acute symptoms, where complete emptying is a diagnostic sign. Sometimes hypophysin or prestigmin was useful for atony of the colon, but the effect was by no means constant. In general, one may say that in no stage of amebic dysentery is there a characteristic roemgen appearance, and there is no special site of involvement. Clinical improvement is accompanied by a corresponding improvement it the roentgen appearance although thickening of the wall of the colon and irregularity of the mucous membrane may persist. The author encountered no cases of stricture such as have been described by Bassler between the sigmoid and the rectum. A recurrence of symptoms should not be carelessly attributed to an exacerbation of the amebic dysentery; a carcinoma was encountered in such a case. Ir. A. Evans, Fr.

Rosser, Curtice, and Kerr, J. G. Cencer of the rectum in young persons. J. Am. M. Ass., Sept. 23, 1939, 113, 1192-1194.

Several writers since 1910 have called attention to an apparently increasing incidence of carcinoma, more particularly carcinoma of the large intestine, in young persons. The authors analyze a series of 100 consecutive cases of rectal cancer to determine the relative incidence of this disease in persons thirty-five tears of age and under, the grade of malignancy present in younger persons as compared with that in more mature years and such other factors as might enter into the prognosis of the younger age group.

In this series 2 per cent were sixteen pears of age, 7 per cent were under thirty and 17 per cent were under thirty-six. The average curation of symptoms for the younger age group was seven months. There was no evidence that the grade of malignancy present in this group was higher in young persons, but colloid cancer was found more frequently and squamous cell cancer less frequently. The younger group provided better surgical risks, and resection was attempted in a greater number than in older persons.

The authors conclude that since this younger group, in contradistinction to some other published reports, does not show a greater percentage of higher grades of carcinoma, it must be assumed that the earlier spread of the lesion, indicated by shorter than average curation of symptoms and early gross involvement of lymph nodes and neighboring structures, is due to a partial absence of defensive barriers

to early spread of the lesions in young persons.—3. G. Henderson.

#### GENITOURINARY SYSTEM

WILL AMS, E. ROHAN. Urography in pregnatey. Brit. J. Radiol., April, 1938, 11, 202-220.

A review of various papers shows that in normal pregnancy the right kidney almost always shows pelvi-ureteric dilatation. Both sides are affected in one-half of the cases, but it is ware to find dilatation only on the left side. Vamous causes of physiological dilatation and advnamia are: (1) obstruction from the enlarging uterus; (2) hypertrophy of the lower urete. In pregnant women without urinary infection a concentric hypertrophy occurs in the lewer zone of the ureter; (3) hormonic influen e. Something in the blood of pregnant women prevents the uterus from emptying itself until full term. While this uterine inhibition is present, so also is there a relative adynamia of the pelvi-ureteric musculature. Urog apac changes in normal cases are: (1) normal excretion rate from kidney; (2) slow pelvi-orereric clearance; (3) moderate dilatation with a column effect from pelvis to ureter.

The changes in pyelitis of pregnancy differ really only in degree from the physiological changes. Six to 8 per cent of pregnant women suffer "pyelitis." In moderate and severe types there may be seen a marked depression of excretory function of the kidneys and marked dilatation, especially of the minor calyces.

The reentgenological diagnosis of placenta praexia should be extremely accurate with the aid o cystography. The bladder is catheterized and empired and 2 to 3 ounces of sodium iodid= are instilled. Roentgenograms are taken in the anteroposterior and the two oblique planes. Moderate downward pressure should be applied to the uterine fundus during exposure. Between the contrast margin of the fundus of the beadeer and the fetal skull outline the total thickness of the translucent space should not exceed 5 to 8 mm. in normal cases. If this soft tissue gate is appreciably widened, it is almost certain that some abnormal structure is present in the weering segment, the walls of which are very thin. This abnormal structure will be eithe: a blood clot or a placenta praevia. S. G. Henderson.

Braasch, William F., and Merricks, James W. Clinical and radiological data associated with congenital and acquired single kidney. Surg., Gynec. & Obst., Sept., 1938, 67, 281–286.

The article, after discussing certain clinical data associated with renal agenesia, emphasizes the more important roentgen data which are:

- 1. The outline of the solitary kidney is larger than the outline of the acquired single kidney or the normal kidney. The incidence of hypertrophy is twice as great and the degree of enlargement, when it is found, is greater.
- 2. The renal pelvis is frequently observed to be enlarged but the relative increase in size does not parallel the parenchymal hypertrophy. This is true in both congenital and acquired single kidney.
- 3. The renal shadow is usually found lower in congenital single kidney than in the acquired type.
- 4. The psoas muscle outline is less sharply defined on the side of the absent kidney in both congenital and acquired single kidney when compared with an unselected group of urograms.
- 5. There is an increase in the width of the psoas muscle on the side of the absent kidney in a few cases of agenesia (16 per cent of cases).

Because the roentgen shadow was normal or only slightly enlarged in 55 per cent of cases of acquired single kidney and in 20 per cent of cases of the congenital type, and because of the variability in the rate of hypertrophy of the remaining kidney after the removal of one, the surgeon cannot rely on the finding of a normal sized kidney at operation to prove the presence of a functioning kidney on the other side.

The cause for the poor definition of the psoas shadow on the affected side may be a matter of atrophy or some disturbance in innervation or lymphatic supply which existed between the psoas muscle and the absent kidney.—P. C. Swenson.

Jupe, M. H. Some observations on cases of suprarenal tumour. *Brit. J. Radiol.*, April, 1938, 11, 242-251.

Primary tumors of the suprarenal gland which are rare compared with secondary deposits may be divided into two groups, cortical and medullary. Cortical tumors may be divided into adenomata and the so-called primary carcinoma of the suprarenal.

The primary carcinoma gives rise to an intra-abdominal mass, and a definite syndrome is seen. Usually, the tumor is found in female children under the age of ten, and gives rise to symptoms of virilism and obesity, producing a picture almost identical with Cushing's basophilism. Obesity with striae in the skin, hirsutes of male distribution, acne and other similar male manifestations may be seen. The urine may contain a male hormone, androsterone. The bones lack calcium as in basophilism.

Tumors of the medulla are generally referred to as neuroblastomata. In accordance with the degree of cell differentiation that has taken place the clinical picture tends to vary. The Pepper and the Hutchinson syndromes are described. The Pepper type affects very young children, the spread is confined to the abdomen, and the course of the disease is rapidly fatal. The first symptom in the Hutchinson type is commonly due to a metastasis, and the commonest site is under the pericranium. Other bones often involved are the ribs, sternum and long bones. An abdominal lump is frequently found. The bone metastases appear as areas of destruction, small and circumscribed, and usually widespread. Raising of the periosteum due to deposits of neoplasm under the periosteum is very common. The findings in 3 cases are given. The constant feature in these 3 cases is the raising of the periosteum of the femora. Congenital syphilis and hemopoietic conditions, such as leukemia and Cooley's anemia are accompanied by periosteal changes and must be considered in the differential diagnosis.—S. G. Henderson.

#### NERVOUS SYSTEM

Davison, Charles, and Wechsler, I. S. Erythroblastic (Cooley's) anemia and neurologic complications (status dysmyelinatus). Am. J. Dis. Child., August, 1939, 58, 362-370.

The authors report a case of erythroblastic anemia which conformed clinically to Cooley's case and subsequently reported cases but which differed from these in the neurologic manifestations which were present. These neurologic findings, such as the mask-like facies, lack of associated movements, pronator signs, hypertonicity and cogwheel rigidity were indicative of lesions in the extrapyramidal system. The status dysmyelinatus of the globus pallidus, the

pigmentary deposits about the ganglion and glia cells of the pallidum and striatum and the Alzheimer glia cells were undoubtedly responsible for the extrapyramidal symptoms. The loss in the usual pigment of the nerve cells of the substantia nigra and locus caeruleus most likely played no part, the authors believe, in the causation of neural signs. They regard the pathologic changes in the striatum and pallidum in their patient as somewhat analogous to those seen in hepatolenticular degeneration (Wilson's disease and pseudosclerosis).— R. S. Bromer.

#### SKELETAL SYSTEM

Anspach, William E., and Clifton, Willie Mae. Hyperparathyroidism in children. Am. 7. Dis. Child., Sept., 1939, 58, 540-557.

Anspach and Clifton report 2 cases of hyperparathyroidism in children. The first case was that of a girl, nine years old at the onset of symptoms, who showed on roentgen examination generalized osteoporosis and metastatic calcification in the soft tissues of the right shoulder and knees. These changes were similar to those reported in hyperparathyroidism in older children and adults. Removal of a parathyroid adenoma relieved the condition and there was no recurrence of hyperparathyroidism during the subsequent three years.

The second case was that of an infant whose symptoms were first noted at the age of three months and progressed for two years. Blindness thought to be due to increased intracranial pressure secondary to distortion and fractures of a soft skull, developed during the second year. Because of the hypercalcemia and hypophosphatemia, together with initial normal renal function, Anspach and Clifton believe that the diagnosis was primary hyperparathyroidism, despite the fact that the sheletal changes somewhat resembled those of renal rickets. The persistent loss of density in the endochondral zones in the roentgenograms indicates, they believe, that acalcification as well as decalcification may be a feature of primary hyperparathyroidism during active body growth.

During the period of observation prior to treatment, while there was persistent hyper-calcemia and increasing decalcification, the serum phosporus value returned to normal. After roentgen irradiation of the neck, the bones recalcified. Polyuria and hypotonia were

relieved. During the two years following irradiation of the neck there was no evidence of dysfunction of the parathyroids. The authors state that this is the youngest patient reported thus far and the only one they know who showed spectacular recalcification following roentzen therapy.—R. S. Bromer.

OPPENHEEMER, Albert. The swollen atrophic hand Zarg., Gynec. & Obst., Oct., 1938, 67, 446-454.

The author describes 14 cases of a peculiar swelling of the bones of the hand associated with atrochy of the skin and interosseous muscles. This syndrome could be correlated with unilateral abnormalities of the intervertebral foramina on the side of the affected hand. The nature of the lesion producing the bony constriction was not specific and did not vary the cinical syndrome. Only ultrashort wave therapy was used over the affected segments with a cure in 6 of 7 patients. The therapy produced no change in the roentgen findings so that the author explains the results as an action on the nerves producing a decongestion of their sheaths. Oblique roentgen projections of the cervical spine are essential to show the lesion - P C. Swenson.

Ecke Walter. Zur Morphologie und Genese des Zweigwuchses; Untersuchungen an Liliputaneri. (The morphology and genesis of warism; examinations of Lilliputians.) Forsehr. a. d. Geb. d. Röntgenstrahlen, August, 1939, 60, 107-134.

The studies were made on II Lilliputians, 9 males and 2 females from eighteen to fortytwo years of age and all members of a dramatic troupe. They varied from 101 to 129 cm. in heigh. In the group were three pairs of siblings. Family his ories revealed that the parents were all of normal size and there was no knowledge of dwarfism among the ancestors. The birth weights were all normal. In the majority of instarces considerable growth in height occurred after the twentieth year. Numerous anthropologic measurements were made on 8 of the Lillinatians and tabulated. The proportions of the body were essentially normal though these was some tendency to brachycephaly and the weight tended to be high in proportion to the height when comparison was made with children of the same size. The facial features were usually childish and in none had the voice changed from its childish character. The genitals were examined in only 2 males and they were observed to be disproportionately small in size and the testes were not palpable. The others gave evidence of extreme modesty and were not examined. There was a general absence of secondary sexual characteristics. The intelligence corresponded essentially to that of a normal adult and they were remarkably reliable in keeping appointments. Blood studies in 4 cases showed a tendency to lymphocytosis (41 to 58 per cent); electrocardiograms were normal in 5 cases.

Extensive skeletal studies with the roentgen ray showed a normal sella turcica in 8 cases and some enlargement over the normal standards of Kovacs in 5. The skeletal development shown in the hands, spine and pelvis corresponded to that of children between five and sixteen years of age. In I case there was shortening of the middle phalanx of the fifth finger which one commonly finds in mongolism, in another an enchondroma of a phalanx was discovered. In 8 of 11 cases there were definite changes in the femoral heads and pelvis resembling Perthes' disease. Aseptic epiphyseal necroses were also observed at the elbow and elsewhere. The development of the paranasal sinuses seemed more retarded than the rest of the skeletal development.

Koch has reported finding cystic degeneration of the hypophysis in a hereditary dwarf and changes have been observed in dwarfed animals. The cystic degeneration may be secondary to some congenital anomaly of the anterior lobe just as goiter forms in hypothyreosis. There follows a review of the literature and a discussion of the possible hypophyseal origin of the dwarfism in this group.—W. A. Evans, Jr.

#### **MISCELLANEOUS**

Meltzer, H., and Kühtz, E. H. Über den Ablauf einen experimentellen Entzündung unter der Wirkung der Röntgenbestrahlung. (The course of an experimental inflammation under the influence of roentgen irradiation.) Strahlentherapie, 1938, 62, 425-435.

The authors attempted to determine the effect of roentgen irradiation on the salt picture occurring in the course of an inflammation. Meltzer has shown by previous experiments that in humans, rabbits and guinea pigs, an in-

flammation produces regularly a considerable displacement in the salts of the inflamed region, the nature of the displacement depending on the given stage in the course of the inflammation and is, therefore, characteristic of the age and of the condition of the inflammation. The method of study pursued by the authors was as follows:

Under aseptic conditions catgut sutures (00) were introduced into the skin of the back of rabbits. Half an hour later the same skin region was irradiated with 825 r (or with fractional doses). After this, one suture with the neighboring skin was excised and examined.

Clinically the roentgen treated skin region differed in no way from a normal skin region into which a catgut suture is introduced under aseptic conditions. In all experiments the wound healed following the excision aseptically. The duration of healing was neither longer nor shorter than in the non-irradiated skin region and the operative scars differed in no way from those obtained in the non-irradiated region.

The hematoxylin-eosin stained histological sections presented a picture of a foreign body inflammation, the picture being dominated by edema and round cell infiltration. After the third day the catgut suture appeared encapsulated by a newly formed connective tissue. Of significance is the fact that on the fifth and sixth day, at a time which was later found to correspond with a definite decrease in the salt content all the phenomena of inflammation had regressed practically completely so that in the pathological sense the suture appeared to be situated in the tissue without practically producing any reaction and being surrounded only here and there by individual round cells and leukocytes, while on the seventh day the infiltration again increased.

Seven hours after the irradiation and after the introduction of the catgut suture, there occurs a definite increase in the salt content and this increase is uniformly distributed throughout the tissue. After this the ash content continues to increase, reaching its highest point on the third day. At this time there has formed a definite ring around the suture which shows an increased concentration of the salts directly around the suture. On the fourth day there occurs a decrease in the ash content and this decrease is most pronounced on the sixth day. At this time, however, the ash particles are again uniformly distributed throughout the skin re-

gion. On the seventh day the salt content begins to increase again.

The behavior of the calcium salt is parallel to the behavior of the total ash content. After seven hours the magnesium content is increased but is definitely decreased after fourteer and after thirty-two hours and again slightly increased on the second, fourth and seventh day. Only a part of the total magnesium salts consist of water insoluble compounds.

From the findings presented above, it is quite clear that under the influence of a single moent-gen irradiation with 825 r the usual course of inflammation is completely changed. Similar changes occur also under the influence of fractional irradiation.—A. S. Schwartzman.

Langendorff, H. Das Verhalten des Retikulozytenwertes der weissen Maus nach Röntgenbestrahlung. (The behavior of the æticulocyte values of the white mouse following roentgen irradiation.) Strahlentherapæ, 1938, 62, 304-314.

According to Coutard the usual irradiation differs from the simple fractional method of irradiation basically by the decrease of the dose per time unit. While in the simple fractional irradiation the dose per minute corresponds to that of the intensive irradiation it equals in the protracted fractional method only about 2-2.5 r. Numerous communications have appeared in the literature regarding the mode of action of both forms of irradiation. In spite of that, even at present it is not quite clear whether the protracted fractional method of irradiation can be substituted by the simple fractional doses. In order to contribute to the solution of this problem, an attempt was made by this author to determine the effect of the various types of irradiation on the behavior of the reticulocyte values of the white mouse. The behavior of the reticulocyte value for purposes of determining the effect of the different types of roentgen i-radiation was utilized because of the fact that previous studies have shown that the number of reticulocytes in the white mouse is usually constant or subject only to slight variations, and because of the fact that even a slight reentgenray dose is sufficient to produce a definite quantitative influence on the reticulocytes. A series of previous studies have shown that a single irradiation of a white mouse with doses of high intensity always produces a definite decrease of the young red cells found in the circulating

blooc. Depending on the size of the dose this phen memor persists for one or more days after which the rumber of reticulocytes returns to normal. When the mouse is irradiated with doses of lesser intensity the time course of the reaction is changed in a given manner. After the adm mis ration of 100 r no demonstrable influence on the erythropoiesis is present; after the Edraini tration of 200 to 400 r, on the other hand, the course of the irradiation reaction takes a longer time when the protracted method is used in comparison with the simple method and a similar dosage. In these cases, therefore, the effect of the protracted dose is greater. A comparison of the curves obtained further shows that under a similar dosage, the radiation intensity increases the effect of the roence rays. This is applicable, however, only for intensities of 1 r per minute. If the dose per time un to however, is below this value, then the time course of the reaction is the same in the two me hocs of radiation application.

When the dose of 1,000 r is divided in such a marker that individual fractional doses of a slight intersity are separated from each other by given intervals of time, then the effect of the roertgen rays on the reticulocyte values is depen lene not only on the type of the time distribution and the height of the fractions, but also on the intensity of the radiation. If 100 r is gives eals then at first no difference in the course of the two reaction curves is demonstrable after the irradiations. If the time interval is increased, however, between the individual irra lia ions, in that 100 r is given at intervals of two days, then the effect of the total dose on the hemopoietic tissue is considerably slighter than that obtained from irradiation with a higaer intensity. Under these conditions the tissues get used to the irradiation and the effect is sess pronounced.

On the basis of the results obtained, it may be stated that judging by the behavior of the reticulacytes, definite differences in the mode of action of the two methods of irradiation exist. The incluence of the simple fractionated treatment can the tissue examined as well as on the entire body is always more pronounced than that resulting from the protracted fractionated irradiation. Nevertheless it must be emphasized that the course of the reaction after a long irradiation requires, in most cases, a greater time interval and that the same total dose is tolerated by the same type of animal to a better extent

than that following a simple fractionating of the dose.—A. S. Schwartzman.

Graham, J. Wallace. Radiation sickness; treatment with nicotinic acid. J. Am. M. Ass., Aug. 19, 1939, 113, 664-667.

In spite of increasing knowledge and improved technique in the use of roentgen rays, radiation sickness continues to be a major problem for those who are using high voltage therapy. The author reviews the literature on this subject. The cause and mechanism of the reaction are unknown and no evidence has been found to support theories regarding such etiologic factors as nitrogen retention and uremia, acidosis, alkalosis, liver damage, hypoglycemia, decreased blood cholesterol, retention of chlorides or injury to the intestinal epithelium. The diverse and sometimes contradictory theories with regard to etiology indicate that the mechanism of radiation sickness is still undefined.

Spies, Bean and Stone noted porphyrinuria in 5 of 7 cases of radiation sickness. Nicotinic acid in doses of from 200 to 1,000 mg. daily was administered to these patients, and the treatment was followed by a prompt cessation of nausea, vomiting, anorexia and headaches in all 7 cases and a return to normal of the urinary porphyrin. This drug was tried in a series of 70 cases under roentgen greatment at the Ontario Institute of Radiotherapy, Toronto General Hospital, including only those cases of radiation sickness in which severe nausea or nausea and vomiting were present. With the onset of the radiation sickness, patients were given 100 mg. of nicotinic acid twice or three times daily, either in the form of powder in half a glass of water and sipped slowly over half an hour, or in the form of 30 mg. tablets administered in a similar manner.

Following nicotinic acid therapy a result was classed as excellent if all symptoms were cured, good if vomiting stopped and some slight nausea remained, fair for cases in which vomiting was decreased to an occasional incident, and failure when the drug had little or no effect. The following table shows the results obtained:

		Rest	ılt	
Area Irradiated	Excellent	Good	Fair	Failure
Abdomen	13	19	4	5
Chest	I	5	3	2
Head and neck	4	7	0	ì
Inguinal gland	0	2	0	0

Head and ab-				
domen	I	0	1	0
Chest and ab-				
domen	0	0	2	0

The mode of action of nicotinic acid has not been determined, but no direct relation to porphyrin metabolism could be shown.—S. G. Henderson.

BAUMEYER, S. Über die Wirkung Kurzwellenbehandlung auf maligne Tumoren. (The effect of short wave treatment on malignant tumors.) *Strahlentherapie*, 1938, 62, 373-375.

Numerous attempts have been made to determine the effect of short wave therapy on malignant tumors. Even though there is no uniformity of opinion on the subject the results obtained by a predominant number of authors were regative.

Haas and Lob have found that short waves show no demonstrable effect on artificially inoculated malignant tumors. If the field strength is increased up to heat coagulation, the reaction of the tumors differed in no way from the reaction of the healthy tissue; these authors were therefore unable to demonstrate any specific biologic effect of the short waves on tumors. Practically identical results were obtained by Collier. These authors have received the impression that tumors treated with short waves showed a somewhat greater growth than nontreated tumors. Pflomm, on the other hand, reported to have obtained a disappearan of artificially inoculated sarcoma of rats following short vave treatment. At this point it must be mentioned that a spontaneous disappearance of sarcoma of rats is occasionally observed. In order to develop a hyperemia and thereby to intensify the sensitiveness of the tumors to roentgen rays, Fuchs subjected to the short wave treatment 2 patients suffering from pulmonary carcinoma prior to the treatment. He believes to have improved somewhat the results obtained in this manner. Urbach and others, on the other hand, advise against the use of short wave treatment in malignant tumors.

This author had an opportunity to study the effect of short wave treatment on a patient and the results obtained by him are summarized briefly as follows:

1. Short waves have a definite influence on malignant tumors.

- 2. Simultaneous short wave and roentgem irradiation may lead to an enlargement of maignant tumors.
- 3. A "sensitization" of tumors to roentgen rays is not obtainable by short waves.
- 4. Short wave treatment of malignant tumors must be warned against.—A. S. Schwarzman.

SMITH, LAWRENCE W., and FAY, TEMPLE. Temperature factors in cancer and embryonal zell growth. J. Am. M. Ass., Aug. 19, 1939, 113, 653–660.

This paper presents clinical, pathological and biological evidence that "temperature" plays one of the most important parts in the activation of embryonic cell growth. Two common principles apparently apply to cellular activity, embryonal cell development and plant germination.

- I. Favorable temperature is the chief activator in cell growth.
- 2. The physical spectrum (from roentgen rays to ultraviolet rays) contains some quality which is inhibitory to cellular growth and regulates maturation and differentiation.

Initial experiments were designed with the simple incubation of fertile eggs at temperatures ranging from 108 to 90°F. for the twenty-one day period usually necessary for the normal hatching of the chick. There is a narrow range between 97 and 104°F., which might be spoken of as the optimal zone, in which normal growth, differentiation and organization of the tissues take place, with the development of a acrmal chick. At the lower level there is a critical temperature lying at approximately 94 or 95°F., at which there will be marked retardation in the development of the embryo and a viable chick will only rarely develop. It is the author's impression, gained from chick experiments, that a temperature just above freezing is not as seriously detrimental to the later normal development of the embryo as is the maintenance of a temperature just below the critical level. In the attempt to demonstrate the importance of temperature with respect to embryonic cell growth, a series of experiments was undertaken, in which the effect of temperature on the growth of normal and cancer cells was studied by tissue culture methods. Preliminary observations bear out the theory that critical levels exist for these cells and that tumor cells are more readily affected by alteration in temperature than are

normal, differentiated, adult type cells. The importance of heat and light with respect to germination, wowth, differentiation and organization of plants is mentioned.

The investigation of the effect of alteration in temperature on the growth of immature, undifferentiated neoplastic cancer cells in human beings was the next step in this work. Thirtyeight patients with inoperable cancer have been treated by local refrigeration alone combined with artificial "hibernation," in which for periods as long as five days the body temperature as read by rectal thermocouple was maintained at levels as low as 85 or 90°F. By refrigeration is meant the application of cold locally by means of ice warer or a brine solution circulated through ar apparatus designed especially to fit the structures in which the lesion exists. By hiber is meant a general reduction of body temmerature below the critical level of 95°F. Through the withholding of food, complete exposure of the body to a constant low environmental temperature (50 to 60°F.) maintained by an air conditioning unit, and light narcos produced with small doses of avertin with arry ene hydrate and of barbiturates, a state of a rificial "hibernation" can be maintained in which metabolism is reduced to an almost accargible figure, with arrest of bowel and renal function. During such hibernation neoplast c les ons are diminished in size even more strikingly than by refrigeration alone. In every instance there has been a prompt reduction in pain. These has been regularly a rapid, gross, measurabæ decrease in the size of the lesion within zwenty-four to forty-eight hours. There has been also a general improvement in the patient's condition, with a gain in weight, a better appetite and a change for the better in the mercal state. These patients had all been giver up from the standpoint of the more orthodox methods: operation and irradiation.

Serial hopsy specimens were taken at varying intervals after the initiation of local refrigeration therapy. Within the first twenty-four to forty-eight hours there occurs a persistent schemia, the effect of continuous cold. Within the first forty-eight hours definite changes in the staining capacity of the tumor cells are frequently found. Within the next few days a descenerative change takes place which ranges from the minimal changes already noted to frank recrosis and complete disintegration of the sele. So long as the temperature locally

is not reduced below an arbitrary figure of 40°F. no demonstrable changes take place in the overlying normal adult differentiated structures such as the skin and subcutaneous tissue.

The authors believe that the application of subcritical temperatures, through methods of local and general "refrigeration," may offer a valuable therapeutic adjunct to our present method of treatment of undifferentiated cell growth, particularly of carcinoma.—S. G. Henderson.

CARTY, JOHN R., and RAY, BRONSON S. Some experiences, experimental and clinical, with direct irradiation of neurological tumors during operation with low voltage radiation. *Radiology*, March, 1939, 32, 325–331.

Avoiding any controversy of the relative value of high voltage and low voltage therapy in cases of brain tumor, the author reports his experience with very low voltage high intensity irradiation in experimental animals and in 12 patients suffering from brain or cord tumors.

The apparatus used was a shock proof machine equipped with various sized cones which could be sterilized. The inherent filtration of the oil in the tube was equivalent to 0.5 mm. Al and the intensity was such that 2,000 r measured in air could be given in twenty minutes at a distance of 20 cm.

Experiments were conducted by irradiating the brains of normal dogs through a window 2 cm. in diameter cut in the parietal bone. Various amounts were given and although all the experiments are not completed it appears that the dog's brain can stand dosages up to 12,000 r at low voltage without showing clinical effects or more than minor microscopic changes. Using larger dosages of 18,000 r it was possible to demonstrate that the depth intensity of the rays is limited and there is comparatively little scattering effect outside the limits of the direction of the beam.

Six cases of brain tumor and 6 of cord tumor, all inoperable, were treated by localizing the beam to the residual tumor as soon after a radical excision as possible; 2,000 r at 60 kv (peak) at 20 cm. distance was given. The only immediate reactions noted were an unexplained fever in 2 of the cord tumor cases and 1 of the

brain cases and a temporary facial palsy developed in 1 brain case.

Sections taken from the tissue in the center of the poentgen-ray beam showed definite tumor cell destruction within twenty minutes after the beginning of the irradiation.

This method of treatment is so new that no conclusions can be drawn as to its ultimate value. In discussing this paper, Dr. Sherwood Moore said, judging from his own experience, he was sure that a great deal of good could be accomplished by this form of irradiation in hopeless cases.—J. H. Harris.

Bromley, J. F. Low-voltage, near-distance x-ray therapy. *Brit. J. Radiol.*, May, 1938, 11, 289-296.

Author's Summary:

- 1. Low-voltage short-distance irradiation has a valuable place in radiotherapy. The limitations of the method must be appreciated, and these are implied in the title. In order to emphasize the essential principle of very short distance, the term "contact" therapy, which was at one time used, would seem to be permissible, even if not strictly accurate. The strict localization of the beam, both laterally and deeply, is an advantage in numerous situations.
- 2. Cooperation with the surgeon will increase the sphere of usefulness for the tube, particularly in mouth and rectal cancer, and possibly in some cases of cancer of the lung.
- 3. Full dosage, founded on careful preliminary measurements, is essential. Administration of a series on an area which has received a previous dose which has proved inadequate is both dangerous and liable to failure. At least 6,000 r must be given to carcinomatous tumors. For rodent ulcer, smaller doses are permissible.
- 4. Multiple small fields directed to the periphery of a tumor are, in general, more efficient than single larger fields. Occasionally, small single fields are permissible in treating rodent ulcer in the canthus of the eye and similar situations.
- 5. An interesting line of research is made possible by the ease with which the beam can be localized to an isolated node of skin cancer, or to a particular portion of tumor.—S. G. Henderson.



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#### BRONCHIOGENIC CARCINOMA

By LLCYD F. CRAVER, M.D.\*

THIS report has a two-fold purpose: first, to emphasize the value of aspiration biopsy in the practical diagnosis of cancer of the lung, and, second, to emphasize the value of roentgen irradiation is the treatment of that disease.

Based on a review (Table IA) of 401 cases in the files for cancer of the lung at the Memorial Hospital, from 1918 to July 1, 1939, the report is restricted to 175 cases that have been regarded as having satisfactory histologic proof of the diagnosis during the years 1920 to July 1, 1939. It is probable that a high proportion of the cases that were not analyzed, 226 in mumber, were also cases of cancer of the lung. but in them there was either no histological material available, or the pathologic diagnosis was so questionable that they were excluded. In addition, there were a few cases in which the evidence strongly suggested that the lung tumor was secondary to a primary carcinoma of some other or-

Age and Sex Incidence. The average age on admission was 53.8 years. By subtracting the elapsed time from apparent enset to admission, the figure for the average age at onset becomes exactly fifty-three years (see Table 1B).

The great preponderance of the male sex found in nearly all studies of lung cancer is strikingly emphasized in this series

TABLE IA

CARCINOMA OF LUNG FILE

MEMORIAL HOSPITAL

Yea:	Proved	Unproved	Total
945	0	4	4
1)4 %	0	8	8
920	I	5	6
192	I	9 •	10
1921	0	16	16
1923	I	6	7
392_	3	5	7 8
192.7	I	14	15
1920	I	13	14
1927	2	9	11
1 )2.3	3	17	20
1924	2	9	11
193*	8	9	17
3-93	10	15	25
133;	9	21	30
:933	18	14	32
193~	20	14	34
193	21	13	34
∃93**	20	9	29
: 93	21	3	24
1934	24	9	33
193≉	9	4	13
	***************************************	office state on the same	
I asals	175	226	401

Note to the low the line, that is after 1932, the number of proved cases subsected the number of unproved cases in each year.

#### TABLE IB

4		
_ Az∷ averag	e) on admission	53.8
Az averag	(e) at onset	53.0

<sup>\*</sup> From the Memorial Hospital, New York. Read at the International Career Congress, Atlantic City, N. J., September, 1939.

(see Table II). For the whole group, the sex incidence was 90.3 per cent in men, 9.7 per cent in women. It was noticed that in the earlier years of the twenty year period covered by the 175 proved cases, this disproportion between men and women was less marked. Therefore, the sex incidence

Table II

BRONCHIOGENIC CARCINOMA; SEX INCIDENCE
IN 175 CASES

Whole group	Men 90.3 €		Že
1920 to 1929	73 - 3	26.7	(15 cases)
1930 to 1939	91.9	8.1	(160 cases)
First half of group	85.1	14.9	(87 cases to May,
Second half of group	95 - 5	4 · 5	(88 cases May, 1935 to July 1, 1939)

was re-analyzed in two ways. For the first ten years, 1920 to 1929, inclusive, the sex incidence was 73.3 per cent men, 26.7 per cent women; while for the second ten years, 1930 to 1939 inclusive, the sex incidence was 91.9 per cent in men, 8.1 per cent in women. Inasmuch as these percentages are based on only 15 cases for the first ten year period, it seemed advisable to compare the sex incidence in the first half of the 175 cases with that for the second half. Here again we find that there seems to be an increase in the greater incidence in the male sex in recent years. Taking the first 87 cases, running from 1920 to May, 1935, the sex incidence is 85.1 per cent in males, 14.9 per cent in females; while in the second half, comprising 88 cases from May, 1935, to July 1, 1939, the sex incidence is 95.5 per cent in males, 4.5 per cent in females.

The significance for the epidemiology of cancer of the lung in these figures, which seem to indicate a changing sex incidence, giving even greater hability to males in recent years, should not be judged until there has been a study of a much larger series from various sources, as our figures

may merely represent an unusual set of circumstances.

### THE DIAGNOSIS OF BRONCHIOGENIC CARCINOMA

Final Proof. The methods by which final proof of the diagnosis was considered to have been made in this series of 175 cases are tabulated in Table III. The methods are arranged in order, according to the likely degree of certainty of proof, beginning with autopsy. Autopsy was done in 34 cases, or 19.4 per cent of the whole group. Tissue removed from a lung tumor at thoracotomy, or an expectorated macroscopic piece of tissue accounted for 10

TABLE III

BRONCHIOGENIC CARCINOMA—175 CASES
METHOD OF FINAL PROOF OF DIAGNOSIS

Method	•	Alone by the Method	mented by Au-	Supple- mented by Other Methods
Autopsy	34	15	SALAKINI PA	19
Thoracotomy	8	7	I	0
Expectorated				
tissme	2	0	I.	1
Bronchoscopy	80	59	11	10
Aspiration of lung	66	58	2	6
Aspiration of rib	I	I	0	0
Aspiration of lymph node	ī	Ī	0	0

cases. In 2 of these cases, the diagnosis was confirmed by autopsy. In 7 cases, or 4.0 per cent, the diagnosis rests alone on tissue removed by thoracotomy.

As for bronchoscopy, the diagnosis rests alone on tissue removed by this means in 59 cases, or 33.7 per cent. In 11 other cases the proof by tissue removed at bronchoscopy was confirmed by autopsy, and in 10 further cases, there was additional histological proof by other means, such as examination of excised nodes involved by metastases or of material aspirated from metastatic tumors in lymph nodes or bone.

As for aspiration biopsy of the lung tumor, it will be noted in Table III that a

considerable proportion of the cases in this series, namely 58 cases, or 33.1 per cent, has been accepted as proved cases of primary bronchiogenic carcinoma on the sole basis, as far as tissue examination is concerned, of specimens removed from the lung by this method.

To critics of the inclusion of 33 per cent of the cases in this series on the basis of tissue removed from the lung by aspiration biopsy, the following statements are made:

It is frankly admitted that in general the bits of tissue removed through a bronchoscope lend themselves somewhat more readily to the skilled pathologist's interpretation of type and grading of carcinoma than do the smears made of material obtained by aspiration biopsy. However, a careful sectioning of the small clots and fragments of tissue obtained with the aspirating needle may yield sections every bit as good and sometimes better than crushed scrapings obtained with a bronchoscope.

The method of aspiration biopsy requires considerable technical experience and cooperation all the way through, including the roentgenological localization of the tumor, the technique of the aspiration, the meticulous saving of every bit of tissue obtained, the careful technique of preparation of slides, and finally the skill of the pathologist in finding significant bits of tissue and in interpreting them.

When on such a basis a diagnosis of carcinoma is made, frequently even as to whether it is epidermoid or adenocarcinoma, and a clinical survey of the patient yields no sign of primary carcinoma elsewhere, one may feel justified in assuming that the case is one of primary lung carcinoma. After all, bronchoscopic removal of carcinoma does by no means make certain that the tumor is primary in the lung, since it is quite possible for metastatic tumors to erode the bronchial wall. The same criteria in judging whether a carcinoma is primary in the lung must be applied in a large measure to cases with bronchoscopic biopsies as to those with aspiration biopsies.

In our series of aspiration biopsies, in addition to the 58 cases in which this method was the only proof, there were 2 cases in which autopsy confirmed the diagnosis and 6 cases in which the proof was supplemented histologically from other sources, such as excised metastatic lymph nodes, aspiration of nodes, aspiration of metastatic lesions in bone, and tissue removed branchoscopically (2 cases).

In one case the histologic diagnosis rests alone upon aspiration of a rib. Since this was a case in which the lung tumor was contiguous to and had directly invaded the rib, it may be considered practically the same as an aspiration of the lung.

In one case the proof histologically rests on an aspiration of a lymph node. With this one exception, all cases in which proof would have to depend on either aspiration or excision of a lymph node have been excluded. This case was included because the tumor was a bulky left apical carcinoma destroying portions of the left first and second ribs and lying very close to the involved left supraclavicular lymph node from which the specimen was aspirated.

As far as proof of primary lung origin is concerned it may be stated that no case can be looked upon with absolute certainty unless an autopsy unqualifiedly demonstrates both grossly and microscopically in the opinion of an experienced tumor pathologistical the the primary site is in the lung. Some autopsied cases have had to be excluded from this report because a review of their material this year showed that they were primary carcinomas of other than broncalal origin.

Proof of Diagnosis for Purpose of Treatment. In Table IV are summarized the methods by which the diagnosis was made in preparation for treatment. Bronchoscopy 80 cases, 45.7 per cent) and aspiration beopsy (64 cases, or 36.5 per cent) are the chief means used in this series to obtain tissue proving that the patient has a carcinoma of the lung before a decision is made about the method of treatment.

It is important to know, if possible, that

a patient has carcinoma of the lung before deciding that he is to be subjected to treatment for that disease since the treatment is severe. The thoracotomies (8 cases, 4.6 per cent) listed in this table were, with one exception, done elsewhere before the patient was referred to Memorial Hospital. As a purely diagnostic procedure, thoracotomy is a rather severe procedure to impose on a patient suspected of having bronchial

#### TABLE IV

BRONCHIOGENIC CARCINOMA; METHOD OF DIAGNOSIS FOR TREATMENT IN 175 CASES

Bronchoscopy	80
Thoracotomy	8
Expectorated tissue (confirmation by this means in 2 cases)	c
Aspiration biopsy of lung	6.4
Lymph nodes excised or aspirated (confirmation by this means in < cases)	_
Aspiration of rib (directly invaded from lung)	7
No tissue during life (all confirmed by autopsy)	
270 dissue during the (all commined by autopsy)	1.5
Total	175

carcinoma. By contrast, bronchoscopy and particularly aspiration biopsy are brief, less hazardous and cause much less delay in subsequent procedures.

The examination of tissue from an accessible swollen lymph node, the seat of metastatic carcinoma, may be of help in proving that the patient has carcinoma arising somewhere within the drainage field of that node, but it is often difficult for the pathologist to determine whether the structure is consistent with origin from lung. The examination of sedimented or centrifuged pleural exudates is notoriously unreliable. Therefore, it is better to avoid if possible relying entirely on evidence from lymph nodes or pleural fluids in making a diagnosis of carcinoma of the lung.

Bronchoscopic Examination. Removal of a biopsy bronchoscopically is preferred to aspiration biopsy in all cases in which it seems at all feasible to have a bronchoscopic examination done. If an actual bit of tissue can be secured through the bronchoscope it is likely to show cellular arrangement and thus to permit a diagnosis of type, grade, and radiosensitivity of the

tumor more readily than the usual aspiration biopsy. The aspiration biopsy may permit only a diagnosis of malignant tumor, more commonly a diagnosis of carcinoma, less frequently a diagnosis of type, such as epidermoid carcinoma, and seldom much information as to grade and radiosensitivity. However, the careful sectioning of the small clot or of gross tissue fragments obtained by aspiration biopsy may yield excellent sections, indistinguishable in some cases from regular sections from routine gross material.

Experience at Memorial Hospital may be somewhat exceptional, in that perhaps some unusually difficult cases for diagnosis have been referred there. Certainly the experience there does not bear out the assertion that bronchial carcinoma can be diagnosed early and with certainty in a very high proportion of cases. As will be seen from Table IV, were it not for aspiration biopsy 64 cases, or 36.5 per cent, of this series would not have been diagnosed, since the use of this method implies that bronchoscopy had failed to obtain proof, or that bronchoscopy was obviously not applicable. The contrast between waiting to have a thoracotomy, or waiting for a tumor to grow along a bronchus so that it becomes accessible, on the one hand, and on the other hand, the obtaining of a diagnosis of carcinoma within thirty minutes by aspiration biopsy, is very impressive to those who have had an opportunity to witness the two experiences.

In 26 cases in which bronchoscopy was done and was negative or had failed to obtain carcinoma (once in 22 cases, twice in 2 cases, three times in 1 case, and four times in 1 case) aspiration was done and obtained the diagnosis.

A reflection of the necessity of relying on aspiration biopsy in order to prove the diagnosis before treatment in many cases in which such diagnosis was not afforded by bronchoscopy or thoracotomy is shown in Table v. Beginning in 1927 and with increased frequency since 1934, it has been found necessary to resort to aspiration.

As one reason for this, a review of the

anatomical locations of the tumors in the lung reveals that a considerable proportion of them lie far out. However, several that were situated close to the mediastinum proved to have no tissue accessible to the bronchoscope. There is a considerable

Table V

COMPARISON OF LEADING METHODS OF DIAGNOSES FOR TREATMENT OF BRONCHIOGENIC CARCINOMA BY YEARS

	Bronchos- copy	Thor-acotomy	Aspiration
1920	l	0	C.
1921	0	1	C.
1922	0	0	C.
1923	0	I	C
1924	I	I	G:
1925	0	1	C
1926	1	0	С
1927	I	0	Ĭ.
1928	1	I	Ĭ
1929	2	0	C.
1930	4	0	I
1931	6	0	3
1932	5	0	3
1933	11	0	3
1934	12	2	3.
1935	10	0	Ģ.
1936	8	0	ıć
1937	<b>\</b> 4	0	15.
1938	9	0	1 <u>3</u> £
1930	4	1	22

group of bulky mediastinal or juxtahilar carcinomas of the lung which apparently arise not from the main bronchi, but from medially situated minor branch bronchi. They may show some compression, fixation, or distortion of the major bronchi, but no accessible material for bronchoscopic biopsy.

In 15 cases in which no histologic proof of diagnosis was obtained during life and in which therefore treatment when given was given with considerable uncertainty, the diagnosis was confirmed by autopsy in all.

The Histologic Types (See Table vI). It was not possible to fit all cases into the commonly accepted three categories of epidermoid carcinoma, adenocarcinoma, and anaplastic carcinoma. Two additional groups had to be made: (1) bronchiogenic

carcinoma n which the growth is undoubtedly of branchial origin, but it is impossible to classify as epidermoid carcinoma or adentifications; and (2) "carcinoma"—a diagnosis often the best that can be made from the bits of tissue obtained by bronchoscopy or aspiration biopsy. Table vi

TABLE VI

\*\*LONCHIOGENIC CARCINOMA

HETOLOGIC TYPES IN 175 CASES

	No.	Per cent
Squarnous and epidermoid carcinoma	85	49
Bronchogensc carcinoma	16	9
Adenocarcinoma	18	10
Anaplastic cascinoma	19	11
"Carci_oma"	37	21
Total	175	100

shows that the squamous and epidermoid group accounts for nearly half the cases, bronchingenic, adenocarcinoma, and anaplastic each for about one-tenth, and the unclassified "carcinoma" for about one-fifth.

Treatment of Bronchiogenic Carcinoma by Irradiation. The study of results of treatment in these 175 cases is based on a follow-up which shows 20 patients living, 140 dead of the disease, and 15 untraced (Table VIII)

Table VII

\*\*\*DNCHIOGENIC CARCINOMA

\*\*POLLOW-UP OF 175 CASES

Living	20
Diec of the disease	140
Lost to follow-up	15
Tetal	175

The methods of treatment used in this series are shown in Table VIII. Two patients referred to Dr. George Heuer and operated on by him and his associates at New York Hospital after the diagnosis had been established at Memorial Hospital (in one by aspiration and in one by bronchoscopic biopsy) are included. Seventeen were not treated. One hundred and forty-two were treated with roentgen rays (200 to 700 kv.) and I were treated by the radon or radium element pack.

175

#### TABLE VIII

## BRONCHIOGENIC CARCINOMA METHODS OF TREATMENT IN 175 CASES Roentgen therapy 142 Radium pack 14 Operation (elsewhere) 2 Untreated 17

Total

Duration of Life in Untreated Cases (See Table IX). Of the 17 untreated cases, 3 were untraced and in one the data are incomplete. In the remaining 13 cases, the total duration of the disease, from the time of apparent onset until death, averaged 14.8 months, and varied from 2.2 to thirty-nine months. Four of these untreated patients survived over two years, assuming that the estimate of the time of onset is correct. It does not seem advisable to try to make a comparison between the dura-

TABLE IX
BRONCHIOGENIC CARCINOMA

Untreated Cases	Follow-up
Living	0
Died	1.4
Lost	3
	***************************************
Total	17

In 13 of those who died, the total duration, from time of apparent onset to death varied from 2.2 to 39 months (4 over 2 years), and averaged 14.8 months.

tion after admission of these untreated patients with the duration after admission of treated patients, since the fact that they were not treated would in general mean that they came considerably later in their course than did the treated patients. However, for the sake of completeness the duration of life in the untreated patients after admission is included here. It averaged 2.4 months, varying from five hours to 11.4 months.

Method of Estimating Value of Irradiation. As a means of attempting to estimate the value of irradiation in palliation of symptoms, the records of all the deceased irradiated patients have been studied and the degree of clinical palliation has been graded on a scale of 0, 1, 2, and 3 (in which

o represents no improvement and 3 represents very marked palliation). Judgment of degree of palliation was made as objectively as possible based on records reporting such factors as gain of weight, lessening or disappearance of cough, hemoptysis, pain, and wheezing, and restoration of the patient's ability to work. At the same time, the duration of life in months following treatment has been recorded.

The cases have been classified by histologic type and by the dose in roentgens estimated to have been delivered to the tumor. In the cases treated by the radon or radium pack, the dose estimated in roentgens must of course be taken with some reservation as to whether it is at present entirely justifiable to compare radium roentgens with x-ray roentgens.

It must further be stated that in these tables (except Table XIB) the dose refers only to that delivered in the initial cycle. Many of the patients in the roentgentreated group had subsequent cycles of irradiation which gave them a much greater total tumor dose than is shown here. These cycles followed at intervals of 1.5 to many months. If one took into account all the radiation delivered to the tumor, one could make out what would seem at first glance to be a strong case for a state. ment that patients receiving the larger total doses showed much better palliation and survived considerably longer on the average (see Table XIB). However, this would be open to at least two objections: (1) those who were in better condition to start with naturally lived longer and could receive more cycles of treatment and therefore a heavier total dose; (2) it is not usually considered proper to add together doses delivered at intervals of several months in computing tumor doses. Of course, the first objection is valid to some extent, even if the dose in only the initial cycle is used, since those in better condition at the beginning are also likely to be able to stand a larger initial cycle. However, the objection seems somewhat weaker in this case, and in the face of the difficult problem

TABLE X
BRONCHIOGENIC CARDINONA

RESULTS IN CASES TREATED BY RADIUM #ACK IN RELATION TO TUMOR DOSE IN ROENTGENS AND EISTOLOGIC TY: E

	0-1000 r				1000-2000 r			
Type	Cases	Paliation	Before	After	Cases	Palliation 0-1-2-3	Before	After
Squamous and epidermoid	3	2	6.6	3 4	I	1-0-0-0	13.0	1.0
Bronchiogenic	3	2-1-0-0	4.7	3 77	I	1-0-0-0	12.5	2.5
Adenocarcinoma	3	2-1-0-0	3.7	2 3	0			
Anaplastic	I	1-0-0	4.3	2 5	0	allow manager,	· more w	
Total	10	7-2-0-0	4.9	3.1	2	2-0-0-0	12.8	1.8
			A.	¥.	en e		A	v.

of trying to gain some proper estimate of the palliative effects of irradiation, it seemed better to reduce the analysis to terms of the roentgens in the initial cycle only, as indicating the degree of thoroughness of the first course of treatment.

The duration of symptoms before treatment is included to try to meet the bjection that cases with longer durations after treatment may have been ones with naturally slower courses. However, this point might be argued two ways: on the one hand, if a longer pre-treatment average is found for those patients living longer after treatment, the objection that they were naturally of slower course could be raised. On the other hand, if a shorter pre-treatment duration is found for those living longer after treatment, it could be argued that on the average, they had ap-

plied for treatment earlier in their course and therefore might be expected to survive longer, whether irradiated or not.

Cases Treated by Radium. Inspection of Table x, showing the cases treated by the radon or radium element pack (at distances from 6 to 20 cm.), reveals that in the 10 cases treated that are suitable for analysis, the results were not at all good. In the light of none recent experience with irradiation, it seems likely that the large radium doses an alled too much irradiation of large sections of the body, in proportion to what could be delivered to the tumor.

Case: Treated by Roentgen Rays. Table XIA shows that as the tumor dose in roentgens is increased in the initial cycle, the duration of life following treatments increases. Cases receiving from 2,000 to 3,000 r in the tamor survived an average of 8.2

TABLE XIA

BRONCHOGENIC CARCINOMA

RESULTS VS. HISTOLOGIC TYPES AND ROENTGENS TO TUMOR INTINITIAL CYCLE IN CASES TREATED
BY BOENTGEN RAWS

Histologic		0-100	o r			1000-20	00 r			2000-30				3000-40	000 r		Term
Type	No.	Palliation 0-1-2-3	Be- fore	After		Palliateen	Be- fore	After	No.	*alliation	Be- fore	After	No.	Palliation	Be- fore	After	
Squamous and	***************************************		general territories	Addison in his begregation of the group			Particular of the San State of	gitteette mage omplete is death		PT I MANAY Interdifficulty following a second configuration and appear							
epidermoid	14	11-2-0-1	12.2	5.1	21	8- 8	12.0	6.4	2.2	4-1C- 7-I	8.6	8.6	2	0-2-0-0	4.5	7.0	
Bronchiogenic	2	0-2-0-0	7.1	5.1	2	2- c-e-o	4.5	2.6	4	2- (- 2-0	15.1	7.9	0				
Adenocarcinoma	ī	1-0-0-0	6.5	0.3	4	3- 1-0-0	12.8	6.3	4	3- C- 1-O	24.2	7.4	1	0-1-0-0	7.8	3.8	
Anaplastic	4	4-0-0-0	11.9	2.4	- 6	3-1-3-1	12.4	5-3	-4	o- 1-0	2.3	6.3	0	***			
"Carcinoma"	7	5-2-0-0	4.6	4.2	7	2- 2-2-0	11.2	7.4	Ę.	o- i- 3-0	11.9	9.0	I	1-0-0-0	5.0	3.8	
	28	21-6-0-1	9.9	4.3	40	18-12-6-1	11.6	6.2	16	Q=1 ≈-14-1	10.7	8.2	4	1-3-0-0	4.4	5.4	
			Α	v.		***	A	V.			A	v.		J	A	v.	

TABLE XIB

RESULTS IN ROENTGEN IRRADIATED PATIENTS NOW DECEASED CONSIDERING TOTAL TUMOR DOSE
IN ALL CYCLES V5. TUMOR DOSE IN INITIAL CYCLE ONLY

		No. of	Palliatio <b>n</b>	Me	onths' Duratio	n
Tumor Dose	Tumor Dose		Cases 0- 1- 2-3		After	Total
Under 1000 r	All cycles Initial cycle	22 28	19- 3- 0-0 21- 6- 0-1	10.1 9.9	3·5 4·3	13.6 14.2
1000-2000 r	All cycles Initial cycle	32 46	17-11- 3-1 18-12- 9-1	12.4	4·4 6.2	16.8 17.8
2000-3000 r	All cycles Initial cycle	29 39	10-14- 4-1 9-15-14-1	8.7 10.7	6.2 8.2	14.9 18.9
3000-4000 r	All cycles Initial cycle	28 4	3- 8-16-1 1- 3- 0-0	11.0 4·4	11.1 5.4	22.1 9.8
(Untreated)		13	Magaziniy	Bef. adm.	Aft. adm. 2.4	Tota

months, as compared with an average survival of only 4.3 months in those receiving less than 1,000 r in the tumor. These figures may be compared with the average survival after admission of 2.4 months in the untreated cases. In the 3,000 to 4,000 r group, as there are only 4 cases (keeping in mind that this represents the initial cycle only) the number seems too few to put any significance on the drop in survival to 5.4 months. Considering either total closes or doses in the first cycles only, there is a marked trend toward improved palliation

as the tumor dose increases (Tables XIA and XIB).

As between the various histological types of carcinoma, there seems to be hardly a significant difference in the survival figures, but the grades of palliation seem to favor the epidermoid group as against adenocarcinoma and anaplastic carcinoma.

adenocarcinoma and anaplastic carcinoma. Results in Living Patients. Of the 20 living patients, one is one of the patients operated on ten months ago by Dr. George Heuer. Although only a right middle and lower lobectomy was done, this patient

Table XII

Eronchiogenic carcinoma
Living patients: results vs. type and tumor dose in roentgens

(in initial cycle)

Tumor dose		1000-20	00 r			2000-30	000 r			3000-400	00 r	
		Palliation 0-1-2-3			Case	SPalliation 0-1-2-3	Be- fore			Palliation 0-1-2-3		After
Squamous and				Transchilde Programme in Indian del								
epidermoid	I	0-0-0-1	30.0	149.9	6	0-3-1-2	11.8	20.1	1	1-0-0-0	13.0	5 · 7
Bronchiogenic		0.000.00	-	ALLTON	2	0-2-0-0	5 · 7	2.1		-	400000	ages harmonical
Adenocarcinoma		2000 To 1800		A400-411	w		district Print	Management, and the second	1	0-1-0-0	9.8	5 · 7
Anaplastic	Mark South and A	and the second of		7000 00 1 100						100 cm = 100		2000
"Carcinoma"	1	0-1-0-0	2.5	6.9	4	0-1-1-2	12.6	26.8	1	0-0-1-0	8.0	4.7
Total	2	0-1-0-1	?	?	12	$\circ$ - $\mathfrak{Z}$ -1-2	11.1	19.3	3	1-1-1-0	10.3	5 - 4
					Victoria	A	v.				A	W.

has gained 60 pounds and seemed free of disease when last seen one month ago. Two of the living patients are of too recent accession to be suitable for analysis. Table x11 shows for the remaining 17 living patients, all of whom were treated by roentgen rays, the data concerning tumor dose in the initial cycle, palliation, and duration in months before and after treatment, just as is shown for the deceased irradiated cases. The shorter duration in some groups of the living patients of course means nothing as yet.

Five, Four, Three and Two Year Servival Rates (See Table XIII). The five year survival rates are discouragingly low. Based on all proved cases regardless of whether treated or untreated, followed or lost, it is only 2.8 per cent. Based on cases treated by roentgen rays it is 3.8 per cent. Even the two year survival rate in cases treated by roentgen rays, the more favorable of the two irradiated groups, is only a little under 7 per cent.

Therefore, we still have to point largely toward palliative effect and possible prolongation of life in an almost uniformly fatal disease in speaking of the value of irradiation in parcinoma of the lung.

These palliative effects are certainly very striking in certain individual instances.

Discussion of Irradiation of Carcinoma of Lung. The evidence here presented suggests that roentgen irradiation is more effective than external irradiation by radium in the treatment of carcinoma of the lung. The figures for palliative results and survival after treatment in the deceased patients indicate the probability of improved results in proportion to the approach to a cancericidal dose delivered to the tumor. It is obvious that, considering even the total dose delivered in repeated cycles over periods of many months, a cancericidal dose has not as a rule been delivered. It may be that there is a threshold limit of tolerance of lung tissue to irradiation beyond which one cannot go without producing undesirable and deleterious effects which might for practical purposes negate the benefits of a control of the cancer process in the lung. It is the studied opinion of the writer, however, that very few indications of such a limitation of tolerance of lung tissue have been seen in this series, and that it is going to be possible, within the mext few years, to deliver safely considerably more radiation to lung carcinomas than has been done in the past. A well chosen plan for cross-

TABLE IIII

BRONCHIOGENIC CARCINOMA
FIVE YEAR, FOUR YEAR, THREE YEAR,
AED TWO YEAR SURVIVALS AS OF JULY, 1939.

(All pat enes surviving over 2 years were treated by roentgen rays)

	All Cases		gen Rays Alone*
p	er∉ent	per cent	per cent
Survivec over five years	2.3	3.1	3.8
Survivec over four years	3-3	3.7	4 · 4
Survived over three years	3.ૐ	4.91	4.8
Survived over two years	5 -4	6.1	6.9

<sup>\*</sup>One p. tiems in this group had a few radium pack treatments.

firing longer target-skin distances, higher voltages, and greater filtration are the technical factors that will permit increased tumor do age.

In recent years at Memorial Hospital, the efforts in treating lung carcinoma have been consentrated chiefly on producing palliation. In numerous cases there is no doubt that considerably more effective irradia icn could have been given in the first cycle which in general offers the best oppositunity for success in treatment. One factor which, I am convenced, has contributed greatly to palliative and growthrestraining effects has been the choice of the size of the portal. As far as possible the persals have been restricted to a field large enough to include thoroughly only the escimazed extent of the tumor, ignoring peripheral shadows on the roentgenogram thought to be caused by secondary atelectasis and inflammatory changes. This

restriction of portals renders possible the delivery of a greater dose to the tumor with less irradiation of surrounding tissue. In this connection, a considerable exercise of judgment is required in distinguishing between shadows probably mostly representing tumor, as in the case of some of the bulky solid carcinomas, and shadows merely representing peripheral atelectasis and secondary inflammatory changes. All the data at hand may be called on to aid in this judgment: the bronchoscopic findings, the films taken after the injection of lipiodol, the films made with heavy exposure, lateral and oblique films, and the finer features of the roentgen shadows.

 $Table\ XIV$   $bronchiogenic\ carcinoma$  Living patients treated by roentgen eavs

	Cases
12.5 years	1 *
4.5 years	2
years	1
2 years	1
18 months	<b>S</b>
6 months	5
under 6 months	5 8
Total	19

Also one patient lost after 2 years was in good condition.

Duration of Life in the Surviving Patients (see Table XIV). Of the 20 living patients, one was operated on at New York Hospital, ten months ago, and is in good condition. The remaining 19 were all treated by roentgen rays. One, who also received some treatment by the radium pack, is alive for 12.5 years.\* Two have survived over 4.5 years (and will probably soon pass the five year mark), one for three years, one for two years, one for eighteen months, 5 for six months, and 8 for less than six months. In addition, one patient lost track of since February, 1939, was in good condition when last seen.

As to the condition of these living patients, all who have passed the three year

mark are up and about, apparently free of evidence of active cancer. The patient who has now survived 12.5 years had considerable necrosis of chest wall two and a half years ago, necessitating surgery and complicated later by empyema. She has recovered fairly well, however, from this complication.\* The two year patient and the eighteen month patient are probably terminally ill. Of the patients with shorter duration, some are in excellent condition, some are ailing moderately, while others are apparently doomed not to survive much longer. Even in the cases of shorter duration, however, all but one showed some degree of palliation.

In surveying these living patients and considering only the five, four, three, and two year survival rates, the net results of irradiation of carcinoma of the lung seem rather disappointing; but an unbiased review of the palliations, some of remarkable degree, that have been witnessed in recent years leads to a belief that at present many more cases of carcinoma of the lung can actually be benefited by irradiation than by surgery at the time when a diagnosis can be made, and that a considerable improvement in results can be expected.

#### SUMMARY AND CONCLUSIONS

As a result of this study it is believed that aspiration biopsy is essential for the earlier diagnosis of a large proportion of cases of carcinoma of the lung, and that treatment of this disease by high voltage roer tgen irradiation can accomplish a great deal in a palliative way, while possibilities of improved technique of irradiation promise considerably improved results in a disease which in the great majority of cases is not suitable for surgical intervention.

I am indebted to Dr. William L. Watson, who has performed most of the bronchoscopies in recent years in this group of cases; to Drs. C. S. Cameron and J. S. Binkley, for their assistance in compiling data from the case records; and to Edith H. Quimby, for her help in computing the tumor doses in roentgens.

<sup>\*</sup> This patient died 9 months later (March 7, 1940).

<sup>\*</sup> This patient died 9 months later (March 7, 1940).

#### METASTATIC NEOPLASMS

#### A CLINICAL AND ROENTGENOLOGICAL STUDY OF INVOLVEMENT OF SKELETON AND LUNGS\*

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#### INTRODUCTION

THE intelligent treatment and prognosis of malignant neoplasms is obviously dependent upon the recognition of tumor cells outside the confines of the primary tumor. Roentgenologic evicence has become a widely used supplement to clinical findings in searching for metastases. Since the skeleton and lungs are the most accessible of various parts of the body, they deserve particular attention in this connection. An understanding of the problem entails a close correlation of involved anatomical and pathological features

In review, the principal types of spread encountered may be listed as follows: lymph-borne emboli; blood-borne emboli; lymph-vessel permeation; blood-vessel permeation; transcelomic spread and various combinations of these methods. One must bear in mind that although emboli and permeation usually occur in the orthograde direction, spread in the retrograde direction of vascular flow is extremely important following obstruction. The channels of spread are further complicated by extensive intercommunication. Grav<sup>13</sup> has recently shown that spread of cancer by lymph-vessel permeation is less common than was formerly supposed.

One or more of the above types of spread has been assumed in cases listed below as metastatic to the skeleton or lungs. Instances of pleural metastases are included with the lung groups. Instances of direct encroachment of the primary tumor into neighboring bone or lung have been avaided even though roentgenographic evidence is frequently similar.

MATERIAL

To accumulate data pertinent to the consideration of metastatic neoplasms, 1,803 hospital records and available corresponding roentgenograms have been reviewed. Caly biopsy proved cases were considered. Among the entire series were 1,303 autopsied cases. All patients considered had been admitted to Pondville Hospital over a ten year period, prior to January 1, 1938. The percentage distribution of bone and lung metastases is furnished by tabulated findings in the autopsied cases. Although tables refer to autopsied cases only, the remarks concerning roentgenographic findings refer to both the autopsied and the other cases proved clinically.

Roemgenography of the lungs and major red bone marrow-bearing areas has been a policy of the Pondville Hospital for the study of all cases of malignant tumors in which clirical evidence suggested spread. In suspected and proved breast cancer this has been a routine procedure. The adequacy of such a film series was reported by Dresser and Pelletiers who found only one instance of bone involvement which would not have been shown in routine studies of the sull, spine, ribs, pelvis and proximal humeri and femora.

For presentation, cases have been arbitrarily arranged in 7 groups to facilitate consideration of various malignant conditions in their appropriate anatomical and pathological divisions.

Group I: Urinary Tract and Male Genital

There were 185 autopsied cases in this

<sup>\*</sup> From the Department of Radiology, Pondville Hospital, Massachusetts Department of Public Health. † Formerly Resident in Radiology, Pondville Hospital.

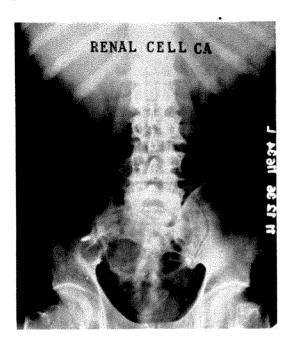


Fig. 1. Roentgenogram showing confident osteolytic involvement of posterior right i ium and adjacent portion of sacrum from renal cell carcinoma. No other bone metastasis.

group (see Table 1). The primary organs involved were kidney, bladder, prostate, penis, testis and urethra.

Table I

URINARY TRACT AND MALE GENITAL ORGANS

Autopsies	Organs	Bone Metastase	Lung Metastases
		per cent	per cent
25	Kidney	20.0	40.0
46	Bladder	13.0	19.5
95	Prostate	57.8	28.4
10	Penis	.0	10.0
5	Testis	20.0	80.0
-1	Urethra	25.0	25.0
185	Total	36.7	28.1

A. Kidney. Most of the 25 autopsied cases of primary renal tumors were renal cell carcinomas and hypernephromas arising in the cortex. Pulmonary metastases were present in 40 per cent and 30ne metastases were found in 20 per cent. These figures are similar to studies reported by a number of investigators in connection with frequency of bone and lung involvement.

Roentgenographic Findings. Many examples of solitary remote and apparently blood-sorne metastases were found in both bones and lungs. Throughout the series a tender cy to form solitary bone metastases often complicated by fracture was observed. Almost all the bone lesions were osteolytic (Fig. 1). Although lobulation of pulmonary metastases from renal tumors has been described, 23 it was not a dependable finding in the films reviewed. Of patients with Wilms' tumor, there was a much greater frequency of metastatic involvement of the lungs than of the bones.

B. Biadder. Forty-six autopsied cases of primary bladder cancer showed bone involvement in 13 per cent and lung involvement in 19.5 per cent. Of 79 autopsied cases collected by the Carcinoma Registry, 4 58 were studied closely by postmortem, and metastatic foci were present in lungs in 25.8 per cent. Graves and Militzer found osseo is metastases in 11.86 per cent of 43 cases

Roentgenographic Findings. Osteoblastic

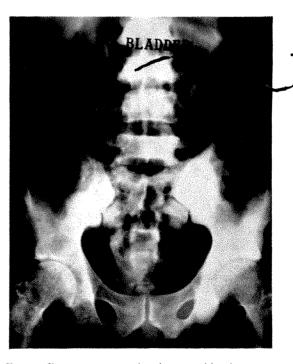


Fig. 2. Roentgenogram showing osteoblastic metastases from carcinoma of bladder. No primary prostatic cancer.

metastases (Fig. 2) were encountered less frequently than osteolytic metastases secondary to malignant bladder tumors. This point is of interest because of the infrequent occurrence of bone-forming metastases secondary to tumors arising in stratified squamous or transitional epithelium. Livingston<sup>22</sup> has reported a similar experience. The pulmonary metastases were widely disseminated in some cases and relatively localized in others.

C. Prostate. In the 95 cases studied by autopsy, 57.8 per cent had bone metastases while only 28.4 per cent had lung metastases. The great predisposition of prostatic carcinomas to form osteoblastic metastases has been frequently recorded. Extensive sectioning by Kaufman<sup>19</sup> resulted in demonstration of bone metastases in 72 per cent of his autopsied cases while Eumpus<sup>2</sup> using roentgenographic evidence alone found bone metastases in only 30 per cent of the cases. Graves and Militzer 5 found lung metastases in 8.6 per cent of cases studied for roentgenographic evidence of metastatic spread.

Roentgenographic Findings. The marked predominance of bone metastases over lung metastases secondary to prostatic cancer is a striking fact since the opposite distribution of metastases is true for most other large groups of primary tumors. Another consistent finding is the more frequent involvement of bones situated near the primary tumor. It seems that other tumors do not so closely obey the principle of direct increase in incidence of bone involvement with increasing proximity to the primary tumor in question. These facts regarding the prostate coincide with the observation of Warren,<sup>27</sup> et al. on the spread of lymphborne tumor emboli along the proportionately numerous perineural lymphatic vessels which drain the prostatic area. Circuitous extension to the neighboring periosteal lymphatics furnishes opportunity for stimulation of bone formation and subsequent extension to medullary bone by means of cortical haversian canals. The presence of bone metastases in 33 autopsied patients of prostatic carcinoma who showed no accompanying lung involvement is chylously out of proportion to the remaining 1,208 autopsied cases of the series which showed only 71 instances of bone metastases without lung metastases. Schmorles reported that prostatic bone metastases may indirectly produce calcium in the lung, presumably because the neoplastic cells incite osteosarcomatous growth in adjacent bone, such as vertebra and ribs. From this secondary metastatic focus embolic cells may produce osteoid tumors of the lung. Willis31 states that stromal metaplastic transformation may occur from epithelial malignancies with the resulting poss bil w of calcium production in pulmonary metastases. However, in the present series, no calcium was detected in prostatic lung metastases. The problem of similarity between advanced metastatic involvement of the pelvis and Paget's disease was encountered several times; however, the discrete osseous metastatic nodules of the former furnish quite a contrast to the accer turted bone trabeculae of condensing disseminated osteoporosis. A significant point regarding the lytic bone metastases of prostatie carcinoma was their greater frequency in the more remote bones, particularly in patients who showed lung metastases and hence, presumptive evidence of blood-stream dissemination.

D. Femic. Of 10 cases of primary carcinoma of the penis, only one, or 10 per cent, had secondary pulmonary involvement. None had osseous involvement.

Rountger ographic Findings. The pulmonary metastases presented no unusual characteristics.

E. Testis. There were 5 autopsied cases in this group of which 4 showed lung involvement and one bone involvement. Twen y-six inoperable clinical cases not autopsied showed roentgenographic evidence of metastases in 53.9 per cent to lung and 12.3 per cent to bone. Stout<sup>25</sup> names lymph nodes, lungs, liver and bones in order of requency of metastatic involvement.

Roentgenographic Findings. Bone metastases were unanimously osteclytic and showed no greater tendency to involve pelvis and lumbar spine than other red bone marrow-bearing portions of the skeleton. In one instance a lytic lesion, several centimeters in diameter, was present in the frontoparietal region with complete destruction of both tables of the calvarium. The lung metastases tended to reach the stage of huge nodulation in marry patients. Incidentally, patients treated for lung metastases from the testis as a group showed the greatest radiosensitivity of all tumors metastatic to the lungs.

F. *Urethra*. Of 4 primary carcinomas, one showed postmortem evidence of pulmonary metastases and one showed osseous metastases.

Roentgenographic Findings Scattered pulmonary nodules were shown in the roentgenogram. The bone metastases were osteolytic.

Comment. Of the entire group of 185 autopsied cases of cancer in u-inary tract and male genital organs, 367 per cent showed osseous metastases and 28.1 per cent pulmonary metastases. As mentioned above, the predominance of bone involvement over lung involvement may be attributed to the pronounced extension of prostatic metastases to neighboring bones through the lymphatics. The greater frequency of bone involvement ir the absence of lung involvement in prostatic cancer further points to the importance of lymphatic extension. In this cornection, the production of osteoblastic metastases from both bladder and prostate suggests a constant influence of lymphatic drainage.

#### Group II: Female Genital Organs.

This group (Table 11) includes 160 cases of vulvar, cervical, fundal, ovarian and vaginal primary cancers.

A. Vulva. Of 10 autopsied cases of cancer of the vulva, 2 showed pulmonary metastases; none showed osseous metastases. Review of the literature produced no reported large series of cases.

Roentgenographic Findings. Chest films showed no distinctive characteristics of the metastases in the lungs.

B. Cervix. Of 99 autopsied cases, bone involvement was present in 8 per cent and lung involvement in 18.1 per cent. In 132 cases, Warren<sup>28</sup> found bone metastases in 3.94 per cent and lung metastases in 15.1 per cent. All bone metastases were osteo-

TABLE II

Autoosies	Organs	Bone Metastases	Lung Metastases
gappangan ang pamanan an Francisco and Arabi Marija Mila Sala Sala Sala Sala Sala Sala Sala S		per cent	per cent
0	Vulva	.0	20.0
99	Cervix	8.0	18.1
32	Fundus	.0	43 · 7
17	Ovary	6.0	12.0
2	Vagina	50.0	50.0
160	Total	6.2	23.1

lytic. A much higher relative percentage of lung and bone metastases were found in histologically Grade 3 cases than in Grades 2 and 1.

Roentgenographic Findings. All of the above bone metastases were osteolytic. There was no striking correlation of the proximity of the metastases to the primary tumor site. The preponderance of spread to bones containing large amounts of red marrow was a definite finding. An interesting example of joint cartilage and capsule acting as a barrier to joint invasion was noted in a patient who showed extensive lytic destruction of the adjacent proximal portion of the tibia (Fig. 3). Varying types of pulmonary metastatic nodules were present in this group.

C. Fundus. Fourteen of 32 autopsied cases of cancer primary in the uterine fundus were found to have pulmonary metastases. No bone metastases were encountered in this relatively small group of cases, however in several cases observed clinically, roentgenograms showed bone metastases. It is interesting that metastases from adenoacanthomas were present in both lungs and bones.

Roentgenographic Findings. The bone metastases which were present were all osteolytic. Instances of pathological fracture were observed. The lung metastases showed no distinctive characteristics.

D. Ovary. In 17 autopsied cases of ovarian cancer, 12 per cent showed lung metastases and 6 per cent bone metastases. Ewing 8 recorded blood-borne pulmonary metastases in 5 to 7 per cent and bone involvement in a somewhat smaller percentage.

Roentgenographic Findings. A clinically observed case showed remote bone metastases near the entrance of the principal nutrient artery of the femur. One case showed pulmonary apical metastatic involvement with late autogenous phrenic interruption. A clinically observed primary ovarian tumor metastatic to the vertebrae showed herpes zoster of a corresponding level indicative of posterior root invasion.

E. Vagina. Of 2 primary vaginal carcinomas, one showed metastatic extension to the bones and one to the lungs. The literature contains few reports regarding the spread of this tumor.

Roentgenographic Findings. No distinctive characteristics were encountered rountgenographically. The bone metastases were osteolytic.

. Comment. Of the entire group of autopsied patients with primary cancer of the female genital organs, 6.2 per cent metastasized to bone and 23.1 per cent to lungs. Regarding bone lesions, it is significant that all were osteolytic and of a distribution compatible in a majority of cases with blood-borne embolic origin.

#### Group III: Oral cavity.

Malignant primary lesions of the lip, alveolar ridge, buccal mucosa, floof of mouth, palate, tongue, tonsil and pharyex were considered in a third group (Table III). Two hundred and eighteen of these cases have been autopsied. As above mentioned, direct infiltrating growth of the primary tumor into bone constitutes a different type of problem. Such occurrences have not been tabulated as metastatic.



Fig. 3. Reenzgenogram showing preservation of knee joint despite extensive involvement adjacent to it. Frimary epidermoid carcinoma of cervix.

A. Lp. Thirty-eight autopsied cases showed osseous metastases in 5.2 per cent. Lung metastases were found in 2.6 per cent. Review of the literature reveals that remote metastases from primary cancer of the lip are quite rare.

TABLE III
ORAL CAVITY

Autopsies	Organs	tastases	Lung Me- tastases
		per cent	per cent
38	Lip	5.2	2.6
10	Alvedar ridge	.0	.0
30	Paiccal mucosa	.0	10.0
20	Hoor of mouth	.0	5.0
14	Palate	7.0	7.0
59	Tomes.e	.0	23.7
21	Torsil	.0	9.0
26	Pharrax	4.0	15.4
218	Total	1.8	11.9

Roentgenographic Findings.\* The bone metastases both in autopsied cases and in clinically proved cases were osteolytic in character and remote in situation. An example was the presence of a fracture at the site of a lytic metastasis in the posterior portion of a rib. The lung metastases showed no unusual roentgenographic features.

- B. Alveolar Ridge. Of 10 autopsied cases of tumors which arose from the epithelium over the alveolar ridges, no metastatic involvement of the lungs, pleura, or skeleton could be found.
- C. Buccal Mucosa. Bone metastases were absent in 30 patients who died of primary lesions of the buccal mucosa. Ten per cent showed lung metastases.
- Roentgenographic Findings. Pulmonary metastases were not distinctive in appearance. One patient showed a pleural effusion evidently the result of metastases.
- D. Floor of Mouth. Of 20 autopsied cases, one patient showed pulmonary metastases. There was no instance of metastatic bone involvement.

Roentgemographic Findings. Disseminated, small pulmonary nodules were observed.

E. Palate. Fourteen autopsied cases of primary malignant neoplasms in the palate gave pulmonary metastases in 7 per cent and bone involvement in 7 per cent or one each.

Roentgenographic Findings. Disseminated pulmonary nodules and osteolytic bone involvement were observed. A compression fracture of a dorsal vertebral body was one example of metastatic involvement of bone. A palatal lesion metastatic to the right cervical nodes was found to have produced right pleural metastases which were obscured by pleural thickening from a large lung abscess.

F. Tongue. A series of 59 autopsied cases included no instance of bone involvement. Lungs and pleura were involved in 23.7 per cent of cases. Ewing<sup>9</sup> has observed repeated metastases from the tongue to the liver, lungs, pleura, heart and adrenal. Willis<sup>32</sup>

found 5 per cent bone and 35 per cent lung involvement. Fuendeling and Hunnicutt<sup>12</sup> found 11.5 per cent of 26 autopsied cases with lung and pleural metastases and 7.8 per cent with bone. The 26 cases were tongue malignancies included in a summary of 1,000 consecutive autopsies of various primary malignant conditions observed at Stanford University Hospital.

Roentgenographic Findings. A relatively high percentage of pleural effusions was found with the disseminated pulmonary metastases.

G. Tonsil. In 21 autopsies, no osseous metastases from primary tonsillar cancer were encountered. Lungs were involved in 9 per cent.

Roentgenographic Findings. Metastatic pulmonary nodules presented no unusual characteristics.

H. Pharynx. Of 26 primary carcinomas ar sing in the oropharynx, osseous involvement was encountered in 4 per cent and pulmonary involvement in 15.4 per cent. The Stanford series<sup>12</sup> included 16 cases with metastases to lungs in 12.5 per cent and to bones in 25 per cent.

Roentgenographic Findings. Bone lesions were osteolytic. Lung metastases were not characteristic.

Comment. In this group of 218 patients, the incidence of bone metastases (1.8 per cent) and of lung metastases (11.9 per cent) is less than from any other group of primary tumors. Hence, extensive roentgenographic investigation may well be reserved for patients who present advanced disease. The relative frequency of pleural metastases even in the absence of pulmonary nodules suggests that lymphatic spread to pleura must often be a factor. To the present, we have seen only osteolytic bone metastases from this group of cases. Willis<sup>33</sup> in 62 cases of primary epidermoid carcinomas found 6.5 per cent metastatic to bones in autopsied cases.

#### Group IV: Gastrointestinal System.

Autopsied cases of primary neoplasms in the esophagus, stomach, biliary tract, pancreas, large bowel and small bowed contributed 391 cases in this general group (Table IV).

TABLE IV
GASTROINTESTINAL TRACT

Autopsies	Organs	Bone Me- tastases	Ling Me-
		per cent	per cent
56	Esophagus	1.8	<b>25.0</b>
107	Stomach	7.4	· . 8
21	Biliary tract	.0	.4.2
16	Pancreas	6.3	35.0
188	Large bowel	11.1	21.2
3	Small bowel	.0	33.0
391	Total	7.9	20.5

A. Esophagus. Of 56 cases, 1.3 per cent showed osseous metastases while 25 per cent showed metastatic extension to the lungs and pleura. Klein<sup>21</sup> found vertebral metastases in 1.75 per cent of autopsied cases. Among 83 autopsied cases it was found that 9.6 per cent were metastatic to lungs and pleura and 2.4 per cent to benes in the Stanford series.<sup>12</sup>

Roentgenographic Findings. Although various types of pulmonary and pleural metastases were observed among autopsied and other cases, one of the most striking examples of miliary distribution of metastases was in this group (Fig. 4).

B. Stomach. One hundred and seven primary malignant tumors of the stomach on autopsy showed bone metastases in 7.4 per cent and lung metastases in 16.8 per cent. Kerr and Berger, 20 in an extensive presentation and discussion of bone metastases in carcinoma of the stomach, found variations of from 1 to 22 per cent reported by various authors from clinical and autopsy surveys. The most frequent sites of involvement were found in the spine, ribs, femora, sternum, pelvis, humeri, skull and sacrum. In 200 autopsied cases of the Stanford series, 12 bone metastases were found in 2 per cent and metastases to lungs and pieura in 29 per cent.

Roentgenographic Findings. Included examples of osteolytic and esteoblastic bone metastases were almost evenly dis-

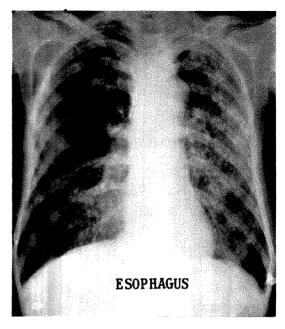


Fig. 4. Reentgenogram demonstrates miliary dismibution of metastatic lesions from primary epicernoid carcinoma of the esophagus. No tuberculos s or silicosis discovered at autopsy.

tributed. In one instance, a metastasis had grown a remarkable amount locally to produce destruction of a portion of the rib marked invasion of the pleura and infiltration of the adjacent lung. Pulmonary metastases were nodular in character, not distinctive in appearance.

C. Britary Tract. Of 21 autopsied cases of primary cancer in the biliary tract, 14.2 per perment metastasized to the lungs. No bone metastases were found. A clinically observed case in a young female presented a mexed osteoblastic and osteolytic lesion in the proximal portion of the right femur.

Rocatgenographic Findings. Pulmonary nodules and pleural involvement were not distinctive in character. The mixed metastatic lesions of the femur mentioned above was predominantly lytic.

D. Fancreas. Sixteen autopsied cases showed bone metastases in 6.3 per cent and lung metastases in 25 per cent. Fuendeling and Hunnicutt<sup>12</sup> found extension to lungs and pieura in 45 per cent of their cases. They reported bone involvement in 7.3 per cent.



Roentgenographic Findings. Pletastatic lesions in ribs, vertebrae, and other bones were osteolytic. Compression vertebral fractures were observed. In one case marked mediastinal broadening was accompanied by metastatic pulmonary nodules and rib invasion.

E. Large Bowel. One hundred and eighty-eight autopsied cases showed bone metastases in 11.1 per cent; lung metastases in 21.2 per cent. In several instances, preliminary roentgenographic evidence resulted in special attention at autopsy to bones not usually included in the routine postmortem examination. Of 156 cases of large bowel malignancy, Warren<sup>29</sup> found 1.2 per cent metastatic to bones and 16.6 per cent metastatic to lungs. Aufses¹ found 8 patients with bone metastases in a group of 117 autopsies. Of 141 cases in the Stanford series,¹² 2.8 per cent metastasized to bone and 16 per cent to lung and pleura.

Roentgenographic Findings. Among bone metastases it is of interest to note that from primary rectal carcinomas, mixed metastatic lesions of pubic rami in 2 instances produced roentgenographic evidence which per se would have been interpreted as osteogenic sarcoma. The bone involvement was predominantly osteolytic. Nodules of varying sizes were found in the lungs in many cases. A case secondary to cancer of the rectum exemplified the consolidated type of pneumonic metastasis in the medial portion of the right lower lobe.

F. Small Bowel. Only 3 autopsied cases of primary cancer of the small bowel were found. No metastatic involvement to bone occurred. In one case lung metastases were present.

Roentgenographic Findings. No roentgenograms were available to show the involved lungs.

Comment. The 391 autopsied cases which contributed to this group showed bone metastases in 7.9 per cent and lung metastases in 20.5 per cent. Osteolytic lesions were the predominant type of bone involvement and in general showed only the pred sposition of location of red bone marrow. Similarity

to osteogenic sarcoma was striking in 2 instances. The lung metastases were of many types. Contrasting types varied from miliary distribution to confluent pneumonic infiltration.

#### Group V: Respiratory System.

Included in this group were 96 autopsied cases of primary neoplasms of nasopharynx, larynx, lungs, trachea and sinuses (Table v).

TABLE V
RESPIRATORY TRACT

Autop- sies	Organs	tastases	Lung Me- tastases
		per cent	per cent
8	Nasopharynx	37 - 5	25.0
41	Larynx	2.4	17.0
33	Lungs and trachea	24.2	45.4
14	Sinuses	7.1	21.4
96	Total	13.5	28.1

A. Nasopharynx. Both in the 8 autopsied cases and in a larger number of clinically observed cases not autopsied, a high percentage of remote metastases occurred. Many of the tumors of this group were examples of undifferentiated primary neoplasm with early and extensive metastases. Of the 8 autopsied cases, 3 showed involvement of osseous structures and 2 had extended to lungs.

Roentgenographic Findings. A typical example of metastatic involvement in bone was noted in the case of a lytic lesion of the sternum. No osteoblastic metastases occurred. There was no discernible relation of the proximity of bone metastases to the site of primary tumor; in fact, the majority occurred distal to the dorsal region. The lung metastases were almost all discrete nodules of varying size.

B. Larynx. Forty-one autopsied cases of laryngeal cancer showed an incidence of spread to bone in 2.4 per cent and to lung in 17 per cent. Burke<sup>3</sup> found no bone metastases in 23 autopsied cases and lung metastases in 8.5 per cent. Burke's study of metastases from squamous cell carcinoma furnisted further demonstration of the

tendency of poorly differentiated carcinomas to metastasize frequently in comparison to well differentiated tumors.

Roentgenographic Findings. Bone metastases were found to be osteolytic. Lung metastases presented no distinctive characteristics.

C. Lungs and Trachea. Of 33 autopsied cases, bone metastases were found in 24.2 per cent. Lung metastases were found in 45.4 per cent. Huguenin<sup>18</sup> quoted various authors to supply the information that remote metastases to some part of the body occurred in 50.8 to 99.7 per cent of cases. Other portions of the lungs, the liver, the brain, and bones have been shown to be the most frequently affected sites. In comparing primary and metastatic lung cancer, Farrell<sup>11</sup> found atelectasis, massive tumor, pleural effusion, hemoptysis and respiratory symptoms to be more frequent in the primary cases.

Roentgenographic Findings. Both osetolytic and osteoblastic bone metastases were observed with a marked tendency to occur in the thoracic cage. Metastases to lobes other than the site of origin of the primary were quite frequent. Pleural metastases were also frequent. Epidermoid and adenocarcinoma showed similar behavior.

D. Sinuses. Of 14 autopsied cases, 7.1 per cent metastasized to bone and 21.4 per cent to lungs. Burke<sup>3</sup> found one example of lung metastases and one of bone metastases among 3 autopsied cases.

Roentgenographic Findings. Bone metastases were osteolytic. Lung metastases presented no distinctive characteristics.

Comment. Of this entire group of 96 malignant respiratory tract tumors, 13.5 per cent metastasized to bone and 28.1 per cent to lungs. In general, it might be said that this frequency of spread justifies more complete roentgenographic observation than is usually conducted.

Group VI: Neuromuscular and Skeletal Systems.

This group included a total of 58 autopsied cases representing primary malignant

lesions of the bone, fibrosarcoma, liposarcomas, malignant melanomas and malignant tumors arising in the nervous tissues (Table vi).

TABLE VI

Autop-	Organs	Bone Metas- tases	Lung Metas- tases
		per cent	per cent
22	Fone tumors	59.0	50.0
ΙΙ	Fibro- and liposarco- mas, etc.	16.1	54 · 5
16	Malignant melanomas	43.7	62.5
9	Nervous system	11.1	11.1
58	Tetal	39.6	48.2

A. Bone Tumors. Of 22 autopsied cases, 59 per cent showed metastases to parts of the skeleton other than the site of origin of the primary. Although this metastatic tendency to other bones was more pronounced in Ewing's tumors, it was found on multiple occasions in osteogenic sarcomas. Fifty per cent of cases showed lung metastases. Willis<sup>34</sup> found one example of metastatic involvement in a remote bone from primary osteogenic sarcoma of the right femur among 4 autopsied cases of this particular malignancy.

Roentgenographic Findings. Metastases to other bones were both osteolytic and osteoblastic in type. The most significant point regarding lung metastases was the occasional formation of calcium in metastatic nodules; presumably, those metastases which were of relatively long duration (Fig. 5) This calcification was not observed in metastases from Ewing's sarcoma to the lungs. Willis<sup>34</sup> found multiple ossifying lung metastases in 1 of 4 autopsied cases.

B. Fibrosarcomas and Liposarcomas. In a group of 11 cases, bone metastases were observed in 18.1 per cent and lung metastases in 54.5 per cent. Other tumors of this general group, particularly myxosarcomas and hemangio-endotheliomas were observed to produce frequent lung metastases and less frequent bone metastases. This was



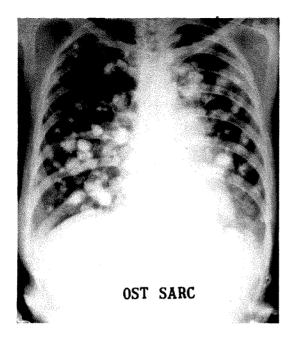


Fig. 5. Roentgenogram showing calcium production of lung metastases. Patient lived nine years following removal of primary osteogenic sarcoma. Steady increase in calcium formed in metastases over period•of several years.

of interest because of occasional histologic difficulty in recognizing potentiality for spread in the latter tumor.

Roentgenographic Findings. Bone lesions secondary to connective tissue sarcomas were osteolytic. Pulmonary metastases were often massive irregular nodules as much as 8 to 10 cm. No ossification of metastatic nodules was observed in this group.

C. Malignant Melanomas. In this group of 16 autopsied patients, bone metastases occurred in 43.7 per cent and lung metastases in 62.5 per cent.

Roentgenographic Findings. Bone lesions were all osteolytic and showed the distribution tendency of major red marrow containing bones. Lung metastases were unusually disseminated and frequently involved all lobes of both lungs. Metastases were found occasionally after the primary lesion had been quiescent for years.

D. Nervous System. Of g autopsied cases consisting of neuroblastomas, neurogenic sarcomas and chordomas, an example of pulmonary metastases was found and one

of bone involvement. Willis<sup>35</sup> found no remote metastases from various primary intracranial tumors. In 2 neuroblastomas, he found lung metastases, one of which also had bone metastases.

Roentgenographic Findings. All bone metastases observed in this group and clinically observed cases were osteolytic in character. A neurogenic sarcoma of the palate by lytic metastatic involvement resulted in a compression fracture of a vertebral body. Lung metastases were most prominent in cases of neuroblastoma of the adrenal medulla. Pleural involvement was seen.

Comment. Of the entire foregoing group of 58 patients, bone metastases were found in 39.6 per cent and lung metastases in 48.2 per cent. Occasionally the intrinsic property of a lung metastasis furnished a clue regarding the nature of the primary tumor. An example of this is found in some of the calcium containing lung metastases from primary osteogenic sarcomas. The film contrast between homogeneous pulmonary metastases from connective tissue tumors and the variable density of those from carcinomas was found to be unreliable in the cases observed in this entire study.

Group VII: Glandular and Hemopoietic Systems.

One hundred and ninety-five autopsied cases supplemented other biopsy proved clinical cases to provide material for this group (Table VII).

TABLE VII
GLANDULAR AND HEMOPOIETIC

Autop- sies	Organs	Bone Me- tastases	Lung Me- tastases
		per cent	per cent
105	Breast	57.1	62.0
8	Thyroid	37.5	60.0
7	Parotid	28.5	42.8
61	Lymphomas	31.1	32.7
8	Leukemias	75.0	12.5
6	Branchiogenic	16.6	50.0
193	Total	46.6	49.7

A. Breast. Of 105 autopsied cases, bone metastases were found in 57.1 per cent and lung metastases in 62 per cent. Of 162 cases, Warren and Witham<sup>30</sup> found 58 per cent metastatic to lungs and 42.6 per cent metastatic to bones. Of 69 cases, metastatic to bone, 41 showed pulmonary metastases. This and other facts resulted in the conclusion that most osseous metastases from the breast are hematogenous. Handley 17 found pleural involvement in 38 per cent of the cases. Gross<sup>16</sup> found pleural involvement in 50.9 per cent, lungs in 49.9 per cent and bones in 20.5 per cent. Of 393 metastases from breast carcinomas, 95.4 per cent were osteolytic according to Sutherland, 26 et al. Extensive dissemination of breast cancer by lymph-vessel permeation as reported by Handley17 seemed difficult to verify in that such cases were shown by autopsy to present blood-steam invasion.

Roentgenographic Findings. Bone metastases were of osteolytic, osteolastic and mixed types. It was of interest that secondary to an "inflammatory" carcinoma of the breast, a previously negative roentgenographic series was followed in three months by a series showing widely disseminated and advanced lytic metastases. Metastatic lung nodules were not distinctive in appearance and were of varying forms. Pleural metastases as indicated by soft tissue prominence following pleural outlines and by the presence of hydrothorax were found in many patients on the same side as was the primary breast tumor and was evidently the result of lymphatic spread. Sx breast sarcomas showed in general similar distribution.

B. Thyroid. Eight autopsied cases showed metastatic involvement of bones in 57.5 per cent and of lungs in 60 per cent. Various estimates gathered from the literature regarding frequency of bone metastases range from 6 to 70 per cent.

Roentgenographic Findings. Bone metastases were unanimously osteolytic. An example was found in destructive involvement of the right femur in its proximal portion complicated by fracture. Metastat-

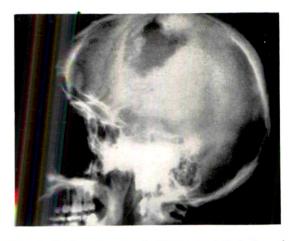


Fig. 6. Roentgenogram showing osteolytic lesion of Hodgkin's disease in parietal bone.

c nodules in the lungs presented no distinctive characteristics.

C. Parotid. Seven autopsied cases showed an incidence of 28.5 per cent bone metastases and 42.8 per cent lung metastases.

Roentgenographic Findings. Bone metastases were all of the lytic type. There was no significant distribution of bone lesions, a good example of which was the presence of a very large lytic area in the ilium. Pulmonary metastases were predominantly large nodules.

D. Malignant Lymphoma and Hodgkin's Disease. Of 61 autopsied cases, bone involvement was encountered in 31.1 per cent (Fig. 6) and intrapulmonary involvement was present in 32.7 per cent. An early report of bone involvement was that of Dresser<sup>6</sup> who in 1926 found more than 4 per cent in cases of Hodgkin's disease. This finding was further confirmed by his later observations. Ewing<sup>10</sup> points to the metastatic character of the growth in the lungs and elsewhere secondary to Hodgkin's disease as evidence for its classification as a malignant neoplasm.

Roentgenographic Findings. The majority of bone lesions were osteolytic although some calcium formation was observed. Recalcification of an osteolytic lesion of the clavicle occurred ten months after roentgen treatment. A neoplastic fracture of the femoral shaft occurred in a patient proved

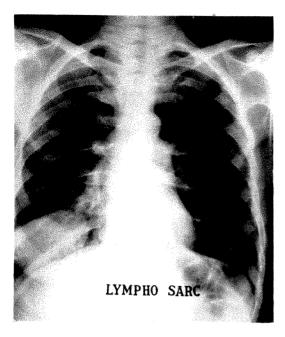


Fig. 7. Roentgenogram showing large discrete-in-repulmonary nodule in lymphosarcoma.

to have lymphosarcoma. Several cases showed solitary discrete nodules in the lung periphery, some measuring as much as \$ cm. in diameter (Fig. 7).

E. Leukemias. Of 8 autopsied cases. 5 were found at postmortem to show leukemic change in cortical bone. One patient showed leukemic infiltration of the peripheral lung tissues.

Roentgenographic Findings. No roentgenographic evidence of leukemic change was recognized.

F. Branchiogenic Tumors. Six patients of this group showed lung metastases in 50 per cent and bone metastases in 16 per cent.

Roentgenographic Findings. Lytic bone lesions were present in the one autopsied case. Lung metastases presented no distinctive characteristics.

Comment. In this group of 195 autopsied cases, lung metastases occurred in 49.7 per cent; bone metastases in 46.6 per cent. The breast constitutes the most potentially metastatic producing single organ of the entire study. The lymphomas metastasized frequently enough to warrant careful ob-

servation. Roentgenographic evidence is unreliable for the study of leukemic involvement of the bone cortex.

#### SUMMARY

Of the 1,303 autopsied cases (Table VIII), 35.3 per cent showed gross or microscopic evidence of extension to lungs or bones. Of these, 26.6 per cent of cases showed lung metastases while 18.4 per cent showed bone involvement. The greater frequency of pulmonary involvement coincides with the position of the lungs as filtering organs. On the other hand, 104 patients had bone metastases in the absence of lung metastases. Such evidence obviously justifies the careful study of bones for metastases even when the chest is uninvolved. The great variety of distribution of metastases can be explained only on the basis of a combination of circumstances. Autolysis of a small or great percentage of cells may occur as they are being transported, or, cells may fail to survive where they lodge, or cells may remain quiescent never to establish focal invasive growth. The transpulmonary passage of tumer cells is undoubtedly a possibility even when foci of neoplasm cannot be demonstrated in the lungs. The unquestionable filtering power of the lungs, liver and regional lymph nodes exerts an influence on the eventual distribution of

TABLE VIII
SUMMARY

Autop- sies	Systems		Lung Metas- tases
	SII (bi), Aut VII a makkaka ada a mara a	per cent	per cent
185	Urinary tract and male		
	genital o≥gans	36.7	28.1
160	Female genital organs	6.2	23.1
218	Oral cavity	1.8	11.9
391	Gastrointestinal tract	7.9	20.5
96	Respiratory tract	13.5	28.1
58	Neuromuscusar and skele-		
~	tal	39.6	48.2
195	Glandular and hemopoietic	46.6	49.7
1303	Total	18.4	26.6

metastatic cells. Still another factor is the consistent predilection of certain primary tumors for certain remote organs, best explained on the basis of intrinsic affinity of given tumor cells for certain tissue.

In the entire series of 1,803 patients, roentgenographic evidence indicated a definite correlation of bone metastases with the anatomical distribution of red bone marrow, i. e., most metastases were found in bones which contained the most red marrow. Prostatic metastases alone seemed to bear a dependable relation to the proximity of the primary tumor, i. e., the nearer the primary, the higher the incidence of bone involvement.

Most metastatic lesions in bone are osteolytic in character. In the present series it seems significant that in no case could an osteoblastic bone metastasis be found secondary to primary malignancy arising in stratified squamous cell epithelium. There were a few instances of bladder (transitional epithelium) malignancies which caused osteoblastic metastases. The osteoblastic metastases in this connection may be related to spread predominantly by perineural lymphatics to periosteal lymphatics.

A tendency was observed for renal neoplasms to produce solitary metastases. Such distant blood-borne metastases were frequently related to a neighboring nutrient vessel entrance.

Roentgenograms subsequent to radiation treatment of osteolytic lesions were found to show calcification more often if the metastasis was definitely radiosensitive than otherwise.

A striking relative immunity of joints in the presence of extensive adjacent meoplastic involvement was frequently observed. This undoubtedly results from the action of the joint cartilage and capsule as barriers to invasion.

In some instances, an increased sedimentation rate and tendency to macrocytic anemia coincided with film evidence of advanced metastatic involvement of bone.

Discrete pulmonary nodules from various forms of lymphoblastoma were not in-

frequent in available films of these cases. These nodules were solitary in some cases and disseminated in others. A definitely greater frequency of pleural extension was found in primary tumors arising above the diaphragm, including head and neck, as compared to those arising below the diaphragm. Many times, cancer of the breast was accompanied by pleural extension on the same side without discrete pulmonary metastases.

The mest dependable intrinsic characteristic of pulmonary metastasis was the presence of calcium in occasional instances where lung involvement was of long duration and primary tumor was osteogenic in origin. Ewing's tumor, because of its different nature, caused no calcium formation in chest metastases.

#### CONCLUSIONS

- 1. Skeletal and pulmonary metastases have been considered in 1,803 patients in an attempt to further orient the present use of roentgenological investigation.
- 2. Bone metastases were distributed in essentially direct proportion to the amount of regional red bone marrow rather than the increasing proximity of the primary with the notable exception of those from the prestate.
- 3. Bood-borne osseous metastases in the absence of lung metastases were of sufficient frequency to emphasize the present clinical trend to search the skeleton for metastases even though the lungs may be negative.
- 4. Except for a minority of bladder cancers, no tumors arising from stratified squamous or transitional epithelium produced estechlastic metastases.
- 5. In several cases, positive demonstration of calcium in lung metastases coincided with the existence of osteogenic primary neoplasms.
- 6. Of malignant conditions arising in nervous tissue, only neuroblastomas, chordomas, neurogenic sarcomas and retinal gliomas produced either skeletal or pulmonary metastases. No bone or lung metas-

tases were observed from primary brain tumors.

7. Greater cognizance is due the fact that various forms of lymphoma may produce discrete intrapulmonary nodules with or without mediastinal and hilar disease.

#### REFERENCES

- 1. Aufses, A. H. Skeletal metastases from carcinoma of the rectum. Arch. Surg., 1930, 21, 916-923.
- 2. Bumpus, H. C. Carcinoma of prostate; clinical
- study. Surg., Gynec. & Obst., 1921, 32, 31. 3. Викке, Е. М. Metastases in squamous-cell carcinomas. Am. J. Cancer, 1937, 30, 493-503.
- 4. Carcinoma Registry of American Unological Association. Carcinoma of bladder. J. Urol., 1934, 31, 423-472.
- 5. Dresser, R., and Pelletier, V. A. Radiological management of cancer of the breast. New England J. Med., 1936, 214, 720-723.
- 6. Dresser, R. Lymphoblastoma (Hodgkin's disease) of sternum. Am. J. ROENTGENOL. & RAD. THERAPY, 1926, 15, 525-529
- 7. Ewing, J. Neoplastic Diseases. Third edition. W. B. Saunders Co., Philadelphia, 1928, p. 827.
- 8. Idem., p. 643.
- 9. Idem., p. 893.
- 10. Idem., p. 406.
- II. FARRELL, J. T., JR. Primary bronched carcinoma and pulmonary metastasis compared clinically and roentgenologically. Radiology, 1937, 28, 445-449.
- 12. Tumor Clinic of Stanford University School of Medicine. Primary carcinomas in relation to metastases. Syllabus for Diagnosis and Treatment of Malignant Tumors, Sept., 1937, p. 10.
- 13. GRAY, J. H. Relation of lymphatic vessels to spread of cancer. Brit. 7. Surg., 1939, 26, 462-
- 14. Graves, R. C., and MILITZER, R. E. Bone metastases from carcinoma of urinary bladder. 7. Urol., 1934, 31, 769-789.
- 15. GRAVES, R. C., and MILITZER, R. E. Carcinoma of prostate with metastases. J. Ural., 1935, 33, 235-251.

- 16. Gross, S. W. Tumors of the Mammary Gland, D. Appleton & Co., New York, 1880.
- 17. HANDLEY, W. S. Cancer of the Breast and its Treatment. P. B. Hoeber, New York, 1922.
- 18. HUGUENIN, R. Le cancer primitif du poumon. Masson et Cie, Paris, 1928.
- 19. KAUFMAN. Quoted by Ewing, ref. 7.
- 20. KERR, H. D., and BERGER, R. A. Bone metastasis in carcinoma of stomach. Am. J. Cancer, 1935, 25, 518-529.
- 21. KLEIN, A. Quoted by Stout, ref. 25.
- 22. LIVINGSTON, S. K. Osteoplastic metastasis in papillary carcinoma of the bladder, Am. J. ROENTGENOL. & RAD. THERAPY, 1936, 36, 312-313.
- 23. RABIN, C. B. In: Diagnostic Roentgenology, Ross Golden, Editor. Thomas Nelson & Sons, New York, 1936, p. 159.
- 24. SCHMORL. Ueber Krebsmetastasen im Knochensystem. Verhandl. d. deutsch. path. Gesellsch., 1908, 12, 89.
- 25. STOUT, A. P. Human Cancer. Lea & Febiger, Philadelphia, 1932, p. 442.
- 26. SUTHERLAND, C.G., DECKER, F. H., and CILLEY, E. I. L. Metastatic malignant lesions in bone. Am. J. Cancer, 1932, 16, 1457-1488.
- 27. WARREN, S., HARRIS, P. N., and GRAVES, R. C. Osseous metastasis of carcinoma of the prostate with special reference to perineural lymphatics. Arch. Path., 1936, 22, 139-160.
- 28. WARREN, S. Studies on tumor metastasis; distribution of metastases in carcinoma of cervix uteri. Surg., Gynec. & Obst., 1933, 56, 742-745.
- 29. WARREN, S. Studies on tumor metastasis; distribution of metastases in carcinoma of large intestine. New England 7. Med., 1933, 209, 167-173.
- 30. WARREN, S., and WITHAM, E. M. Studies on tumor metastasis; distribution of metastases in cancer of the breast. Surg., Gynec. & Obst., 1933, 57, 81-85.
- 31. WILLIS, R. A. The Spread of Tumours in the Human Body. J. & A. Churchill, Ltd., London, 1934, p. 168.
- 32. Idem., p. 416.
- 33. Idem., p. 418.
- 34. Idem., p. 436.
- 35. Idem., p. 441.



#### TOMOGRAPHIC STUDY OF CANCER OF THE LARYNX<sup>1</sup>

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MONTEVIDEO, URUCTAY

THE progress in the treatment of cancer of the larynx has brought about a better knowledge of its clinical aspects and a more accurate conception of the point of origin of the tumor and of its extent before any treatment is decided upon.

The laryngoscopic examination remains the basis of the diagnosis but it does not always give an idea of the real extent of the invasion of the tumor. Also, in some cases

Fig. 1. Frontal tomogram of a normal larynx, showing the free edge of the epiglottis with both pharyngo-epiglottic folds (above), the two descending aryepiglottic folds, false cords, Morgagni's ventricles, both vocal cords, subglottic and tracheal lumen.

the laryngoscopic examination may, for some reason, be difficult and give little information.

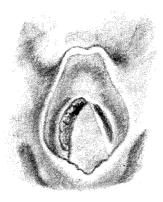
In 1922, Coutard<sup>2</sup> devised and developed the coentgenographic examination of the pharynx and larynx by means of a profile plate. This has been of great value in determining the extent of tumors of the hypopharynx. In the larynx the profile roen genogram is very useful in tumors of the interior subglottic region, of the laryngeal wall of the epoglottis, and of the



Fig. . Drawing of Figure 1. The glottic and supraglottic lumen resembles a club of playing cards. Exernally the pyriform sinus and then the thyroil cartilage (in black). Below (also in black) on both sides of the first portion of the trachea, the critical.

<sup>&</sup>lt;sup>1</sup> Read before the Philadelphia Chapter of the Pan-American Medical Asseciation, April 5, 1939.

<sup>&</sup>lt;sup>2</sup> Coutard. Note preliminaire sur la radiographie du laryax normal et du aryax cancereux. J. belge de radiol., Vol. 13, p. 287.



Ftg. 3. Tumor of Morgagni's ventricle invading the false cord, the vocal cord and the subglottis of the same side.



Fig. 4. Frontal tomogram of same case as Figure 3, showing invasion extending from false cord to subglottic and narrowing externally the pyriform sinus.

anterior commissure—in other words, in those tumors in which the development is more important on a sagittal plane. In contrast to this, these profile projections are not of great value in determining the extent of tumors of the false cord, lateral subglottis—in other words, tumors in which the development follows a frontal plane.

Several attempts have been made to obtain frontal roentgenograms of the larynx; the superposition of the spine was the first obstacle. The technique which consisted in

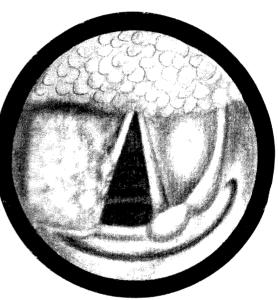


Fig. 5. Tumor of the epiglottis treated by surgery. Recurrence on right false cord and arytenoid.

the ntroduction of a narrow film down to the nouth of the esophagus does not have any practical value.

Ir 1936, I started working with the tomographic examination of the larynx<sup>3</sup>

3 A. d. aten. de clin. quir., July, 1936.

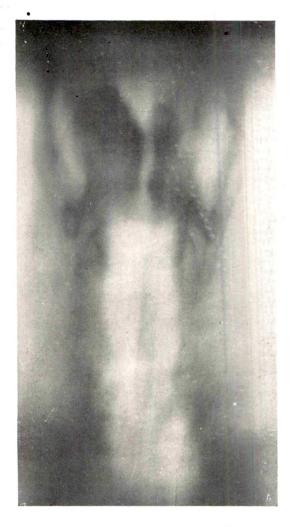
LEGENDS FOR FIGURES 6-9 ON NEXT PAGE.

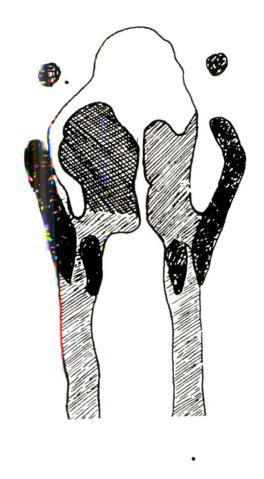
Fig. 6 (apper left). Tomogram of same case as shown in Figure 5. Laryngeal lumen altered. The heavy she dow of the tumor is evident.

Fig. 7 (upper right). Drawing of Figure 6.

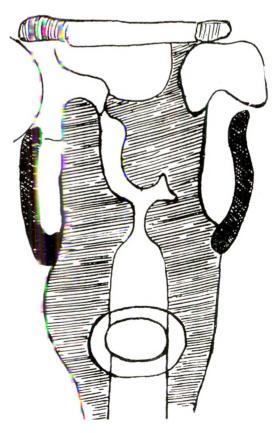
Fig. 3 (lower left). Frontal tomogram of an advanced case of tumor of the false cord.

Fig. 2 (lower right). Drawing of Figure 8.









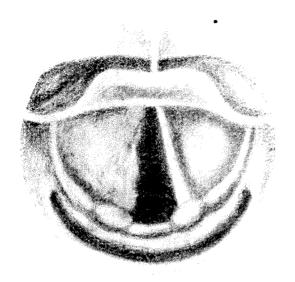
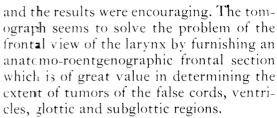


Fig. 10. Tumor of right false and true cords on a tuberculous larynx.



Tomography does not replace any of the previous methods of examination of the larvex, but rather complements them.

In the course of our study of tumors of the larynx we have had the opportunity of considering a few cases of laryngocele or hernia of Morgagni's ventricle. In those cases tomography seems to be of diagnostic value, especially in the cases where the hernia remains in the larynx and may simulate a tumor. Tomography shows the pres-



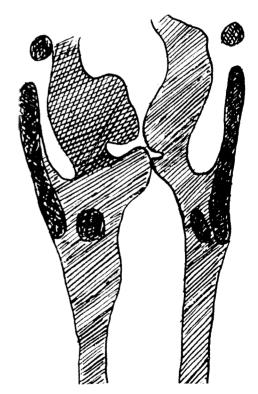


Fig. 12. Drawing of Figure 11.

F13. 11. Frontal tomogram showing enlargement of right false and true cords, narrowing of the ventricle. Left ventricle almost invisible due to edema as confirmed by intervention.



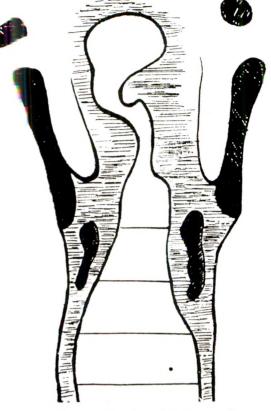
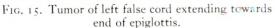


Fig. 14. Drawing of Figure 13.

Fig. 13 (left). Frontal tomogram of a case of advanced tumor of the larynx, showing considerable change and deviation of the laryngeal lumen.

ence of an air cavity and may show its communication with the ventricle, even though this is exceptional. The laryngocele may be accompanied by a malignant tumor and simulate an extension of it. In 5 cases which we have observed, one remained after radiotherapeutic treatment of a malignant growth of the subglottis, and another remained after treatment of a tumor of the false cord, giving the impression of a non-sterilization of the tumors.

<sup>4</sup> This is a case of Dr. Coutard's, studied with him at the Chicago Tumor Institute.





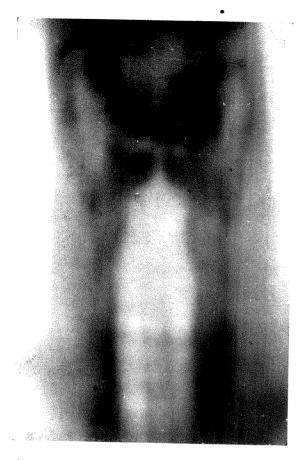


Fig. 16. Frontal tomogram of same case shown in Figure 15. Heavy shallow of tumor of left false cord and narrowing of ventricle. The pyr form sinus is also narrowed.

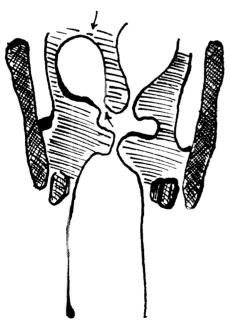


Fig. 13. Drawing of Figure 19.

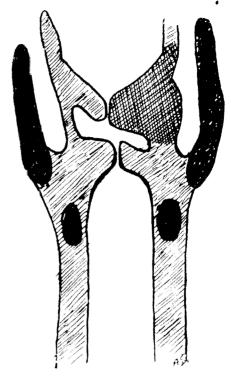


Fig. 17. Drawing of Figure 16.

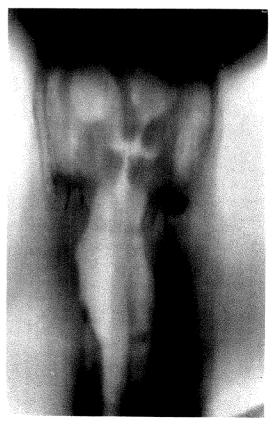


Fig. 19. Frontal tomogram of a case of laryngocele showing communication with the ventricle,

The interpretation of a tomogram of the larynx is not difficult, but it is necessary to obtain good films to avoid errors of interpretation. The plane of the tomogram must be accurately parallel to the axis of the organ; the films otherwise obtained may give false impressions of the presence of tumors. To be of value, the tomographic examination must be frontal; the films thus taken give a valuable point of comparison

of both sides of the larynx.

In the interpretation of tomograms one should follow the symmetry or asymmetry of soft tissues of both sides of the larynx in their relation to the cartilages.

Every case examined by the tomographic method should have had a previous laryngescopic examination and a profile roentgenogram.



# THE VALUE OF NITRITES IN CARDIOSPASM (ACHALASIA OF THE ESOPHAGUS)\*

#### PRELIMINARY REPORT

Boston, Massachusetts

3y MAX RITVO, M.D., and EUGENE J. McDONALD, M.D.

THE purpose of this communication is to describe a means of abolishing the esophageal obstruction which occurs in cardiospasm. This can be accomplished in many instances by the use of amyl nitrite or nitroglycerine. The administration of these drugs usually results in partial or total disappearance of the stenosis of the lower end of the esophagus permitting free passage of fluid and food into the stomach. The patient obtains relief from the distressing symptoms associated with the cardiospasm and the roentgenologist is enabled to perform accurate studies of the esophagus and the remainder of the gastrointestinal tract, which he cannot do satisfactorily in the presence of a marked degree of esophageal obstruction and dilatation.

#### CLINICAL AND ROENTGEN ASPECTS

Cardiospasm is an idiopathic dilatation of the esophagus with a constant or intermittent contraction of the cardiac portion or lower end of the esophagus. No anatomic stenosis is demonstrable and the origin and mechanism of the malady are not clearly understood. It has been thought to be due to a great variety of conditions, among which may be mentioned the following: cicatrices and adhesions in the region of the lower esophagus; endocrine imbalance: neuroses; abnormalities in the diaphragm, liver tunnel or the left lobe of the liver; kinking of the lower esophagus; reflex irritation from cancer of the stomach, peptic ulcer, appendicitis, pulmonary disease, etc.; degenerative changes in the vagus nerve with predominant activity of the sympathetic nervous system. From the large number of etiological factors ascribed to this condition, it is obvious that probably no one of them alone is the true causative factor. Most of the explanations of the cause of cardiospasm are based on the assumption that there is a constant, spasmedic contraction of the esophagus which fails to relax for the ingress of food. However, there is a great mass of clinical and experimental evidence which indicates that no actual spasm exists, or that at least spasm s not the sole factor, in many cases of card ospasm.

The present view, which is gaining everwidening acceptance, is that the condition is due to a defective or absent relaxation of a normal tonicity rather than to a spasm. The passage of a bolus of food down the esophagus induces sensory impulses which normally result in a lessening of the tonus of the lower end of the esophagus, permitting passage of the food into the stomach. Failure of this normal mechanism of deglutition results in dysphagia, stenosis of the inferior portion of the esophagus and dilatation above the point of obstruction, the syndrome known as cardiospasm. The condition is, therefore, one of failure of coördination of the muscles of the lower esophagus and the esophageal wall. The term achalasia, which means absence of relaxation at the proper time, is the correct one rather than cardiospasm, which should be discarded and has been retained by us only because it is historically well established and universally used in the literature. In some cases, the entire esophagus dilates markedly and there is actual hypertrophy of its walls, which, nevertheless, fails to overcome the obstruction. Achalasia of the esophagus is believed to be analogous to Hirschsprung's disease, which

<sup>\*</sup> From the Boston City Hospital, Boston, Massachusetts, Department of Reentgenology, P. F. Butler, M. D. Roentgenologist-in-Chief. Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19-22, 1939.

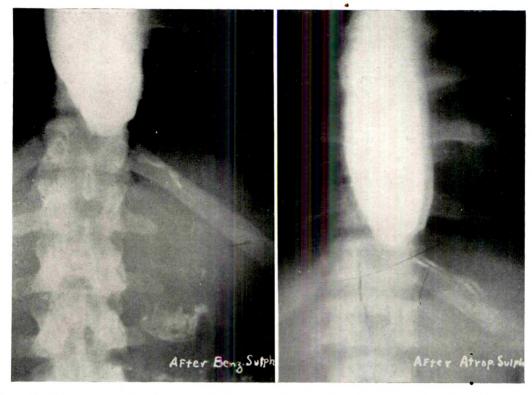


Fig. 1. Cardiospasm, unaffected by benzedrine or atropine. A. B., male, aged twenty-three. Has suffered with severe dysphagia for seven years. Occasional periods of partial relief, but is never completely free of symptoms. Bougies have been passed with slight temporary improvement. Roentgen examination revealed marked dilatation of the esophagus with stenosis of the lower end. After the administration of benzedrine and atropine sulphate, there was no relief of the operation.

is due to an imbalance of parasympathetic and sympathetic influences.

Clinically, achalasia of the esophagus is of importance because it is next in frequency to carcinoma in producing the symptoms of esophageal obstruction. Dysphagia, pain in the chest, and regurgitation are the major complaints in patients suffering with this condition. A feeling of weight under the sternum, belching and vomiting of undigested food are common. Progressive loss of weight with severe malnutrition and dehydration may ensue in severe, long-standing cases.

In addition to the suffering caused by the cardiospasm, the obstruction may be a source of much annoyance to the roentgenologist. On roentgen study, the diagnosis rests on the demonstration of a smooth, conical stenosis at or near the cardia with dilatation, often of a very marked degree,

above it. Fluid and food particles may result in obscure shadows; also, the esophageal obstruction may interfere with roentgen examination of the stomach, duodenum and intestines as will be discussed in detail below.

#### DLUGS USED IN OUR STUDIES

A means of abolishing the esophageal stenosis is, therefore, greatly to be desired, not only for the benefit of the patient in relieving his distressing symptoms but also because of the increased ease and accuracy with which roentgen studies may then be carried out. Several drugs were tried without success. Atropine, which has been recommended for many years as an antispasmodic, was found to be totally ineffective even when used in large doses to the limit of physiological tolerance. The bromides and belladonna proved disappoint-

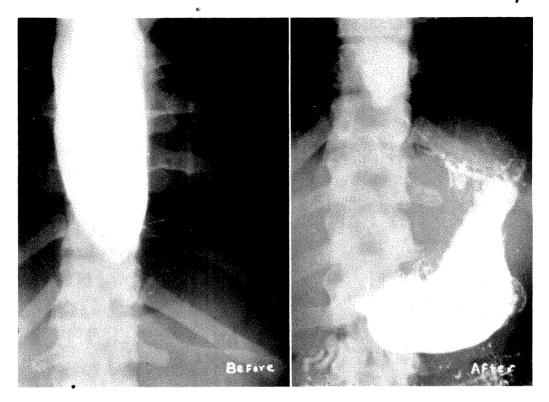


Fig. 2. Cardiospasm, relieved by nitrog yeerine. A. B. (same patient as in Fig. 1). "Before" shows the esophageal obstruction and dilatation. After the administration of 17100 grain of nitroglycerine, the stenosis disappeared and the esophageal contents emptled into the stomach. The patient stated he was aware of the removal of the obstruction.

ing. Benzedrine, which is useful in spasm of the pylorus and intestines1, produced no relaxation of the lower end of the esophagus in doses up to 30 milligrams (Fig. 1). Various combinations of the above drugs also proved ineffective. Because of the relaxation of the ampulla of Vater and other spasms3 produced by amyl nitrize, we carried out experiments with this drug. The effects were gratifying. After the inhalation of the vapor, there occurred in most instances an almost immediate disappearance of the stenosis of the lower end of the esophagus with passage of the esophageal contents into the stomach. However, this drug proved not to be the ideal agent for our purpose because it not infrequently caused unpleasant side-reactions. Tablets of sodium nitrite and erythrol tetranitrate were then tried; the effects were slight and very variable. Nitroglycerine was next used and was found to produce satisfactory

results in most instances. Doses of 1 100 grain were given to the average patient, very thin or obese persons receiving slightly smaller or larger amounts (Fig. 2). A factor which is of great advantage with nitroglycerine is that this agent is effective by absorption from the floor of the mouth wher the tablets are held under the tongne. This is of particular importance in the condition under discussion as the esophageal obstruction results in delayed absorption and consequent ineffectiveness of drugs administered orally in the usual manner. It also avoids the necessity of injection methods, which are objectionable because they may limit the usefulness of the treat nent.

# METHODS OF STUDY AND EFFECTS OBSERVED

Patients were given the barium mixtures used in the routine examination of the

esophagus. Roentgenoscopic observations were carried out and films taken in the erect position when possible. If cardiospasm was present, the site and degree of obstruction and the extent of the dilatation were noted. Other abnormalities in the esophagus and neighboring organs were carefully sought for. Deep-breathing exercises, reassurance of the patient, and repeated examinations were made to rule out transitory spasm and to establish the constancy of the condition. Then the drug was given. The patients were not told which drug was being used nor what effects were expected. Placebos of saccharum lactis tablets were used at times to rule out purely psychic effects. With amyl ni-1. trite, the pearl was crushed and the patient instructed to take several deep inhalations of the vapor. The nitroglycerine was administered in the form of the soluble hypodermic tablet, 1/100 grain; the tablet was placed in the floor of the mouth and allowed to dissolve under the tongue, the patient being instructed not to swallow for as long as possible.

After the amyl nitrite inhalation, the effect was usually almost immediate. With nitroglycerine, the esophageal obstruction began to disappear in from thirty seconds to but or five minutes. In some instances, the lover end of the esophagus showed definite filatation with continuous and rapid passage of the esophageal contents into the stomack (Fig. 3); in others, the barium mixture passed downward in a series of spurts with short periods of stenosis intervering between the spurts. In those instances in which the drug was effective, the patients experienced relief and were aware of the removal of the obstruction. The ingestion of more of the opaque meal indicated that the duration of the effect persisted from a few seconds to several minutes after which time the stenosis reestablished itself as previously. The effect on the Leart was very dramatic as observed roentecoscopically. The cardiac pulsa-

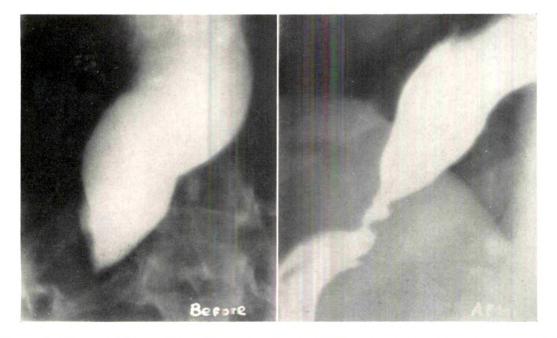


Fig. 3. Cardiospasm. Relief of obstruction by nitroglycerine. P. R., male, aged twenty-four. Acute onset of esophageal obstruction about three years ago. Esophagoscop howed no organic lesion. Passage of bougies resulted in temporary relief. Roentgen studies (before) showed marked dilatation of the esophagus with stenosis at the cardia. After the administration of 1/10c grain of nitroglycerine, the stenosis disappeared and the esophageal contents passed rapidly into the stomach.

tions became very rapid and of diminished amplitude and the heart shadow appeared to decrease in size. As the effect of the drug wore off, the heart gradually returned to its previous state.

The effects of amyl nitrite were prompt in nearly every case in which we administered this drug. Nitroglycerine was more

# THERAPEUTIC EFFECTS OF THE NITRITES

The effects of continued administration of nit-oglycerine were observed in 6 cases in order to determine whether the drug had value as a curative agent. Doses of 1/200 grain were given three or four times daily for periods of from three to ten days. On

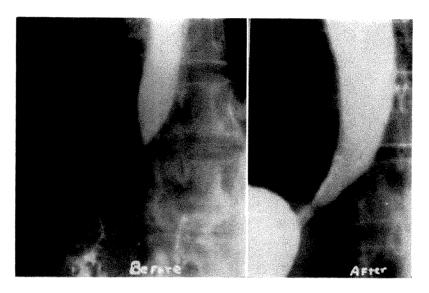


Fig. 4. Cardiospasm, before and after nitroglycerine. G. O. D., female, aged forty-eight. Gradual onset of dysphagia about three years ago with increasing difficulty during past four months. Roentgen examination prior to giving nitrites revealed marked narrowing of the lower esophagus with almost complete obstruction and moderate dilatation above. After 1/100 grain of nitroglycerine was given, the lower esophagus dilated and the entire esophageal contents flowed into the stomach.

variable and less effective, yet proved more satisfactory for routine use. It has been used in 14 cases with partial or complete abolition of the stenosis in II instances. Some of the patients were given the drug on numerous occasions. Roentgenoscopic observations were carried out each time. Increased or repeated doses were used when necessary without serious ill effects. In order to obtain satisfactory roentgenograms showing the effects of the drugs, it is essential that the roentgen machine be equipped with a rapid change-over device so that "spot films" may be exposed rapidly while the patient is under roentgenoscopic control (Fig. 4).

re-examination, the obstruction and dilatation of the esophagus were in every instance found to be present as previously. Admiristration of another single dose of amyl ritrite or nitroglycerine at the checkup observation after the period of taking the drug again usually resulted in a temporary disappearance of the stenosis. Smaller doses of nitroglycerine, 1/300-1/50c grain, were then administered to a small group of patients every three or four hours throughout the day for several days. The results proved disappointing. Moreover, the patients in some instances tolerated the drug poorly and suffered unpleasant reactions from even these smaller doses.

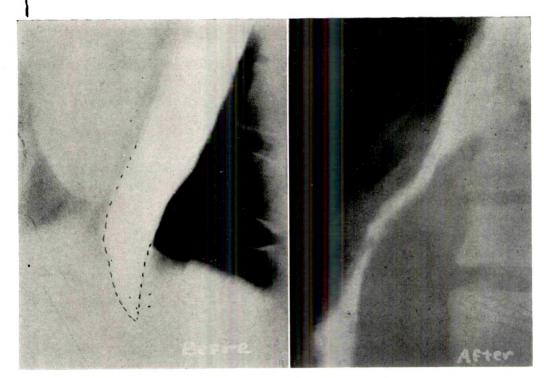


Fig. 5. Cardiospasm relieved by nitrites. E. McK., female, aged thirty-six, married. Acute onset of dysphagia four and one-half years ago. Now states she cannot swallow liquids or solid food, has marked substernal pressure, and vomits frequently. Bouginage has resulted in relief for short periods. The film before giving the drug (retouched) showed complete esophageal obstruction with dilatation of the esophagus. After the inhalation of amyl nitrite, the stenosis disappeared and the opaque mixture flowed into the stomach.

Although the nitrites have proved of no permanent curative value in the true sense of the word, the drugs do nevertheless have a definite though limited application in the treatment of cardiospasm. Patients with severe, chronic achalasia of the esophagus may lose much weight and become severely dehydrated; apprehensiveness with fear of food frequently becomes a factor of serious import; vomiting and regurgitation with choking and severe coughing may cause pulmonary complications. In acute attacks of obstruction, the patient may actually struggle for breath and become cyanotic in attempting to dislodge a bolus of food by violent straining. Temporary relaxation of the stenosis may prove a lifesaving procedure in cases of this type, and this relief can frequently be obtained with amyl nitrite or nitroglycerine. Cardiospasm is in many instances associated with neurotic symptoms and a vicious cycle is thereby set up. The breaking of this theoretical cycle by the demonstration that the obstruction may be abolished by these agents may start the patient on the road to recovery in that it removes from his mind the idea that he is afflicted with a hopeless condition from which he can expect no relief. In the treatment of cardiospasm, the passage of bougies may in some instances be facilitated by the use of nitrites just prior to the operation, as the dilatation produced by the drug permits the instrument to pass through the lower esophagus and the danger of perforation or trauma to the esophageal wall is lessened.

#### VALUE OF ROENTGENOLOGY

To the roentgenologist, the nitrites are

of definite value and serve to increase the ease and accuracy of the roentgen studies of the gastrointestinal tract in cases of cardiospasm. These patients may retain large amounts of fluid and food particles in the esophagus, frequently for long periods of time. Little or none of the opaque mixture required for the roentgen studies

and patients with achalasia of the esophagus may present other complaints which make complete roentgen studies of the gastrointestinal tract very desirable. Similarly, disease in the esophagus itself may be overlooked or incorrectly diagnosed in the presence of marked obstruction. Food particles retained in the esophagus produce

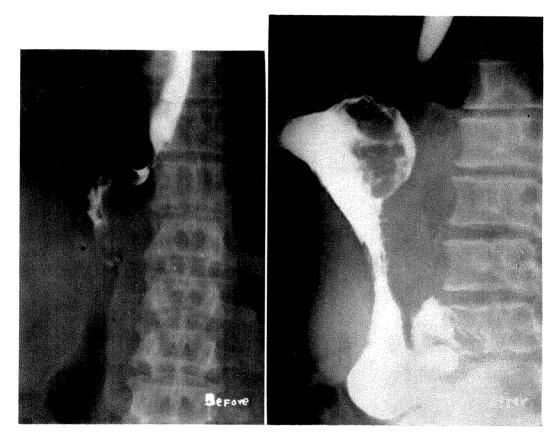


Fig. 6. M. McK., female, aged sixty-nine. Difficulty in swallowing both solid and liquid foods for several weeks. Roentgen studies revealed a stenosis of the lower erd of the esophagus. The obstruction was so marked that the patient could take only small amounts of the opaque mixture. Carcinoma of the esophagus was suspected, but satisfactory examination was impossible. After the administration of 1/100 grain of nitroglycerine, the esophageal obstruction disappeared. An extensive neoplasm of the cardia of the stomach without involvement of the lower end of the esophagus was 4 monstrated.

may flow into the stomach because of the stenosis, so that satisfactory visualization of the stomach and intestines becomes impossible. It is recognized that carcinoma of the cardia or fundus of the stomach may be associated with esophageal obstruction (Fig. 6); peptic ulcer and other abdominal lesions may similarly produce cardiospasm;

mottling or filling defects which are easily confused with carcinoma. The fluid in the esophagus causes dilution of the barium mixtures and may obscure ulcers, neoplasms, diverticula and other esophageal lesions. Disease processes in the mediastinum, neart, lungs and dorsal spine may be overlooked or misinterpreted because of

the confusion resulting from the overlying shadows of the dilated, fluid-filled esophagus. Attempts to eliminate these difficulties have previously required esophageal lavage or dilatation by bougies. It is simpler, safer and more satisfactory from the point of view of both patient and physician to avoid these procedures by the comparatively simple expedient of administering amyl nitrite or nitroglycerine.

#### SIDE-EFFECTS

The nitrites are very prone to cause unpleasant reactions. With amyl nitrite, the side-effects may be marked and definitely limit the usefulness of the drug. The pungent odor is very objectionable to many patients. Giddiness and fainting with complete loss of consciousness occur frequently. If the patient is erect, which is the preferable position in the roentgen study of the esophagus, he is very apt to faint and fall to the floor. This drug is therefore best used with the patient recumbent, careful watch being kept for reactions. Patients with severe coronary disease or angina should be given amyl nitrite with caution. In no instance were there any serious after-effects in our cases, and we feel the drug may safely be used within the limits mentioned above.

Nitroglycerine also produced untoward reactions; however, they were milder and less troublesome. Flushing and perspiration were the most common ill effects. Nausea and vomiting were apt to occur. Throbbing and pounding headaches, giddiness and vertigo were present in many patients. Fainting occurred rarely. In none of the patients were these reactions serious and many persons suffered no ill effects from single doses. A striking fact is the extremely wide variation in tolerance of different individuals.

#### SUMMARY AND CONCLUSIONS

Cardiospasm is an idiopathic stenosis of the lower portion of the esophagus with marked dilatation above the point of obstruction. The condition is believed to be due to a defective relaxation of the normal tonicity rather than a spasm and should more properly be termed achalasia of the esophagus.

There has previously been no satisfactory method of abolishing the esophageal obstruction except by mechanical dilatation.

The administration of amyl nitrite or nitroglycerine produces a disappearance of the stenesis of the esophagus in many cases of cardespasm, permitting the passage of fluid and food into the stomach.

The abolition of the obstruction in those cases in which the drug is effective gives the patient relief from his distressing symptoms; it permits of accurate roentgen visualization of the esophagus and the remainder of the gastrointestinal tract; the passage of dilators may be facilitated and the cargers of traumatism or perforation during instrumentation lessened.

The effect of the drugs is of short duration; nevertheless these agents appear to have a definite though limited application in the meatment of cardiospasm.

We wish to express our appreciation to Dr. P. F. Butler, Forntgenologist-in-Chief at the Boston City Hospital Boston, for his cooperation and assistance in the preparation of this paper.

#### REFERENCES

1. Merson, A., and Ritvo, M. Benzedrine sulfate and its value in spasm of the gastro-intestinal tract. J. Am. M. Ass., 1936, 107, 24-26.

2. McG was, J. M., Butsch, W. L., and Walters, W. Pessure in the common bile duct of man; its relation to pain following cholecystectomy.

7. Am. M. Ass., 1936, 106, 2227–2230.

3. Holmes, G. W., and Dresser, R. Use of amyl nitrite as an antispasmodic in the roentgen examination of the gastrointestinal tract. Am. J. Econtgenol. & Rad. Therapy, 1928, 19,

#### DISCUSSION

Da Fierard B. Capps, Chicago. Very little has beer written regarding the use of nitrites in card capain, and I think that Drs. Ritvo and McDonald have shown that they have a very definite place in this condition. It is well known that atropine and related compounds are ineffective in those types of cardiospasm which we may call "achalasia." Hearst, Cameron, Wright

and others, have been fortunate enough to have had the opportunity of examining histologically a number of these cases and they have been able to demonstrate the anatomic reason for this fact. They have found in practically all of such cases a destructive lesion involving Auerbach's plexus of nerves. Since the vagus nerve acts through this plexus on the smooth muscle of the esophagus, atropine would not be expected to have any effect. Furthermore, the normal relaxation of the cardia at the end of swallowing would not be expected to occur. Nitrites, on the other hand, since they act directly on the smooth muscle, would still be effective.

These cases Hearst called "achalasia of the cardia," simply meaning failure to relax. These are the cases that show the most pronounced symptoms and findings both clinically and roentgenologically, namely, marked dilatation of the esophagus and very marked dysphagia. Clinically, however, there is a large group of other cases that are termed cardiospasm where dysphagia is not such an important finding, where pain is perhaps the presenting symptom. Such patients frequently do not show any ab-

normalities on roentgen examination and atropine is usually a successful therapeutic agent.

I should like to reaffirm Dr. McDonald's remarks concerning the bad effects of nitrites. I do not believe they will prove very satisfactory as regular treatment for cardiospasm. In the first place, as he stated, they have a very transient effect. There is no permanent benefit. The discomfort associated with them is frequently too great to make them satisfactory and, finally, in a great many cases we have other more satisfactory forms of treatment. As a diagnostic procedure under the fluoroscope they undoubtedly are extremely valuable.

I should like to reaffirm one other statement that syncope not infrequently occurs in certain individuals following the use of nitrites. Although this is not a serious situation in younger persons, there are a great many older people where it might result rather seriously and I think this should be taken into consideration. Of course, if the patient is not in an erect position, syncope is not so likely to occur and immediately putting him in the prone position will usually bring relief.



### CHARCOT'S ARTHROPATHY OF BOTH ANKLES\*

#### CASE REPORT

By S. A. LEADER M. D.

Veterans\* Administration Facility

NORTH CHICAGO, ILLINOIS

TABETIC arthropathy has been known since Mitchell called attention to it in 1831. It was not until after Charcot's criginal description in 1868 of the destructive joint lesion which has come to bear his name that the condition began to receive wide recognition. Since then numerous case reports as well as detailed discussions of all phases of the subject have been published. Just to cite a few pertinent to the present report:

Charcot himself in 1873 noted the occurrence of spontaneous fractures in tabes; Steindler, in a series of 64 cases of neuropathic joints, found 11 spontaneous ractures including one of the astragalus; Stewart, in his recent article, included a case of bilateral involvement of the astragalus.

It is merely intended to submit a brief case history with illustrations which should be of interest because of the unusual opportunity afforded to follow the progress of the condition from its inception to the july developed state.

#### CASE REPORT

H. G., white male, aged forty-six, was admitted to the Veterans' Administration Eacility, North Chicago, Illinois, on March 26, 1936. He had been under observation at various Veterans' Administration Facilities since 1932 when he was treated for an injury of the right great toe. In 1910 he had contracted gonorhea and a primary genital chancre. On Marel 29, 1932, the blood Wassermann was 3+ and the Kahn 2+. He was accordingly given a course of antiluetic therapy consisting of bismuth and arsphenamine. On July 14, 1932, blood Wassermann was negative and the Kahn I+, but a neurological examination revealed fixed pupils, sluggish knee jerks, and absent ankle jerks. The diagnosis of early tabes dorsalis was made.

(Spinal puncture was refused.) Another course of artilue ic treatment similar to the first was administed.

Between June, 1933, and July, 1934, patient worked in a C.C.C. camp. Then he began to have shooting pains in the legs and swelling and inflammation of the feet in the warm weather. In August, 1934, he was confined to bed for about four weeks with "rheumatism." Finally, on November 15, 1934, he was again hospitalized by the Veterans' Administration. At this time his ankles were enlarged and somewhat tender, but motion was full. There was a severe degree of pes planus, bilaterally. A roentgenogram taken November 16, 1934, revealed no evidence of bony changes of the feet or ankles, but the medial aspect of the right ankle was rather prominent (Fig. 1). Blood, spinal fluid, and Wassermann were negative. The Lange collodal gold test was not satisfactory. There were three cells per cubic millimeter of spinal fluid. He was given a full three months' course of mercury rubs, bismuth, and tryparsamide.

On April 23, 1935, he was sent to the Soldiers' Home for domiciliary care and he remained there until September 14, 1935, receiving another course of bismuth and tryparsamide during this period.

On September 20, 1935, he was again hospitalized. He complained of pain in the feet on standing and walking. A marked prominence of the inner aspect of both ankles, especially the right, was noted. A roentgenogram taken September 27, 1935, showed separation of the posterior process of the left astragalus and destructive changes of the posterior process of the right astragalus and irregularity of the right navicalar bone (Fig. 2). By December 31, 1935, the condition had become more pronounced so that on roentgen examination a medial dislocation of the right astragalus was seen (Fig. 3). There was marked relaxation of all the ligaments. At this time a diagnosis of early bilateral Charact's disease of the ankles was made. He was again given antiluetic therapy consisting

<sup>\*</sup> Published with permission of the Medical Director, Veerans' Administration, The assumes no responsibility for the opinions expressed or the conclusions drawn by the writer.



Fig. 1. November 16, 1934. A, dorsoplantar and B, lateral roentgenograms showing no demonstrable bone changes.







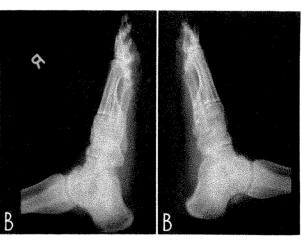


Fig. 2. September 27, 1935. A, dorsoplantar roentgenogram showing beginning medial displacement of right astragalus and area of rarefaction of left. B, lateral view showing destructive changes in each astragalus and irregularity of right navicular.

of a complete course of bismuth and tryparsamide, and part of another course.

He developed mental symptom: so that the

diagnosis of taboparesis was made and on March 26, 1936 he was transferred to the hospital at North Chicago, Illinois. On admission

Fig. 3 (*right*). December 31, 1931. Displacement and rarefaction are more marked.

Fig. 4 (below). March 31, 1936. A, dorsoplartar roentgenogram showing spontaneous (patho-





logic fracture of right astragalus, with dislocation. L, leteral view showing involvement of posterior articular surface of right calcaneus as well as right astragalus.







Fig. 5. Photograph showing deformity at present.

he complained only of his feet being tired when he stood on them any length of time. He was partly disoriented, somewhat euphoric, and lacked insight. Essential neurological findings were fixed pupils, sluggish knee jerks, and absent ankle jerks. The Romberg sign was only suggestive. Vibratory sensibility and deep pain were decreased over both ankles, more so on the right. However, muscle and position sense as well as pain and temperature were retained. There was marked deformity of the right ankle, as is shown in Figure 6, but no tenderness. Roentgenogram taken March 26, 1936, revealed a fracture dislocation of the right astragalus, an area of rarefaction in the left astragalus, and early destructive changes in the right calcaneus, in addition to the changes previously noted. Spinal fluid and blood Wassermann were negative. Lange colloidal gold test was 0012333210. He was given intensive antiluetic treatment which included three full courses of bismuth and tryparsamide and full doses of potassium iodide, as well as malarial therapy.

There has been little change in the condition of the ankles other than an increase in density of the right astragalus. This is demonstrated by the ast roentgenograms taken on March 5 and 8, 1938. Various orthopedic appliances have been used and at present the patient still tires if he is on his feet too long, but he is fairly comfortable with the use of an appliance which protects the medial aspect of the right ankle. Surgical measures have not been considered advisable by the orthopedic consultants. His mer tal condition has improved somewhat so that the principal manifestation is now a somewhat defective memory.

#### DISCUSSION

The following points should be noted:

(1) Tabes was recognized clinically as early as 1932. In July, 1934, patient began to complain of his feet and legs, but at no

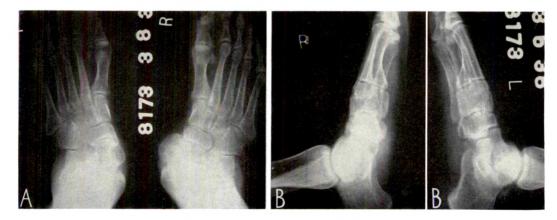


Fig. 6. Latest roentgenograms. A, March 8, 1938, and B, March 5, 1938, demonstrating increased density of right astragalus.

time was there any history of acute severe symptoms referable to the right ankle.

- (2) Patient received a number of courses of antiluetic therapy before any bone lesions were demonstrable on the roentgenogram; yet the destructive bone changes developed and progressed rapidly so that in less than a year and a half after a negative roentgen finding, there was a marked deformity of the right ankle. The experience of other observers has been more favorable, however. For example, Alajouanine was able to secure improvement after involvement of the cuboid and navicular bones was already demonstrable by roentgen examination.
- (3) Unfortunately, no spinal fluid examination was available before antiluetic therapy had been given. However, one spinal fluid examination in 1934 and two in 1936 gave a negative Wassermann reaction.

Steindler, quoting a number of other observers, states that spontaneous fracture may be the first sign not only of arthropathy but also of tabes itself and that an interval of two to three years between the spontaneous fracture and the initial tabetic symptoms is not uncommon. In this case, the clinical findings of tabes were present about four years before the fracture was demonstrated.

While the onset of the Charcot's joint is frequently sudden, as described by Stewart and others, yet many cases of insidious onset have been reported, as in the present case.

I wish to acknowledge my appreciation to the hospital authorities for the aid extended in securing material and also to thank Mr. Robert Heth and Mr. Ray Dornfeld who prepared the photographs and prints.

#### REFERENCES

- 1. ALAJORANINE, T., BASCOURRET, M., and MAGE, J. Larthropathie tabétique médiotarsienne. Bull et mém. Soc. méd. d. hôp. de Paris, 1931, 47, 1-75-1284.
- 2. Barker, L. F. The Neuropathic Arthropathies.

  Mongraphic Med., 1920, 4, 116.
- 3. Castellen, L. I. M. Case of Charcot's disease in joints not commonly affected. *Lancet*, 1931, 2, 1022-1023.
- 4. CHARCON. Leçons sur les maladies nerveux. New Sydembam Series, 1868, 4th Lesson.
- D NOAM, J. H. Neuropathic arthritis. J. Am. M. Ass., 922, 79, 1987.
- 6. Expesser, L. A sign occurring in cases of tabes complicated by Charcot's joints. J. Am. M. Ass., 621, 77, 604.
- 7. Heddes. P. C., Phemister, D. B., and Brunschwes, A. In: Diagnostic Roentgenology.

  Ross Golden, Editor. Thomas Nelson & Sons.

  Wew Work, 1936, pp. 468-474.
- 8. Hoogsom, N., and Whyte, A. H. Charcot's casease of ankle joint. Newcastle M. J., 1927, 7. 144-146.
- KNAGGS, R. L. The Inflammatory and Toxic Liseases of Bone, William Wood & Co., New York, 1926, pp. 105-119.
- 10. Maroz, ▓. H. Charcot's foot. J. Am. M. Ass., 1428, ₪, 846.
- 11. Markowers, E. Röntgendiagnostik der Knochenund Gesenkerkrankungen in Tabellenform. G. Thiente, Leipzig, 1929, p. 89.
- PEMBERTSEN, R. Arthritis and Rheumatoid Condizions. Lea & Febiger, 1935, p. 392.
- 13. Philips, H. B., and Rosenbeck, C. Neuroarthropathies, a consideration of etiology and general characteristics. J. Am. M. Ass., 1924, & 27.
- 14. STELWDLEE, A. Tabetic arthropathies. J. Am. M. A.S., 1931, 96, 250-256.
- 15. STEWART, D. M. Roentgenological manifestations in Done syphilis. Am. J. ROENTGENOL. & Rad. Theerapy, 1938, 40, 215-223.
- 16. TOPEREOFF, N. N. Collateral factors in origin of talletic steo-arthropathy. Sovet. med. vostoch. Sieiri, 1931, 1, 83-90.
- 17. WILE, U. ∰, and BUTLER, M. G. Critical survey of Charact's arthropathy. J. Am. M. Ass., 19,55, 9 € 1053-1055.



#### TRAUMATIC PNEUMOCRANIUM

#### A REPORT OF TWO CASES\*

By ROBERT P. BARDEN, M.D., D.Sc. (Med.)

A CCIDENTAL introduction of air into the cranial cavity was first described by Chiari in 1884. In the American literature, a comprehensive review of this subject was presented by Dandy<sup>1</sup> in 1926. Smith and Malcolmson<sup>2</sup> stated that 43

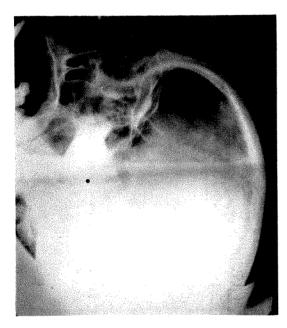


Fig. 1. Case 1. Lateral view with roentgen beam horizontal. Made immediately after death. The large collection of air beneath the frontal bone is well seen. The anterior cerebrum is compressed. There is a fluid line passing through the sella turcica. This was the condition found on the portable examination the day after admission.

cases had been described up to 1931. Madigan<sup>3</sup> and Taft<sup>4</sup> each contributed a case report subsequently.

This communication presents 2 additional cases with this rare condition and emphasizes a point in the technique of its roentgenographic demonstration.

Case 1. J. A., white male, aged fifty-five, was brought to the hospital by police on November

1, 1938. He was stuporous and had been drinking. The only history available was that he had fallen down a flight of stairs a short time before admission. On examination, his pupils were found contracted, and the ocular movements uncoördinated. There was a serosanguineous discharge from the right ear. Blood pressure 130/90. No other neurological findings.

Fortable roentgen examination the next day showed evidence of an extensive fracture through the base of the skull, probably involving the nasopharynx. There was a large collection of air within the skull which shifted with change in position of the head. This was considered a pneumocranium with the air in the subdural space.

The patient never regained consciousness. Temperature and pulse steadily climbed, and he died on the third day after admission.

An autopsy was performed by the coroner. Ar. extensive fracture of the base of the skull was found. One part of the fracture ran upward

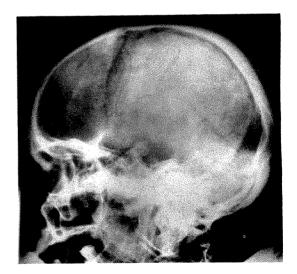


Fig. 2. Case 1. Lateral view with roentgen beam vertical. Made immediately after death. Although the pneumocranium is still well seen, the fluid line has disappeared. It is possible that small collections of subdural air would fail to show in this projection.

<sup>\*</sup> From the Department of Roentgenology, Allegheny General Ho-pital, Pittsburgh, Pa.

and backward from the foramen magnum to involve the occipital bone. The other ran upward and forward from the foramen magnum involving all the structures of the base and traversing the sphenoid sinus and the sella turcica to end in the posterior nasopharynx.

CASE II.\* C. W., a white male, aged fifty-eight, shot himself through the right temple on October 13, 1938. He was found semi-conscious in his room several days later and was brought to the St. Francis Hospital on October 21. On examination, he was stuporous but could be aroused. He was blind in both eyes with evident intraocular hemorrhage in the right. No other neurological signs.

Roentgen examination the same day showed a bullet just inside the left zygoma with a train of lead dust extending back of the orbits to the hole of entry in the right temporal bone. In the

\* Presented through the courtesy of Dr. Leslie H. Osmond, Radiologist at St. Francis Hospital, Pittsburgh, Pa.

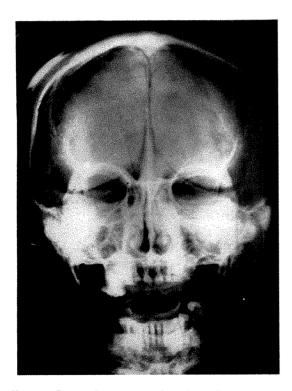


Fig. 3. Case 1. Posteroanterior view with roenegen beam vertical. Made immediately after death. The subdural air has shifted with change in position of the head and now outlines the cerebral hemispheres. A part of the fracture lines is seen near the midline.

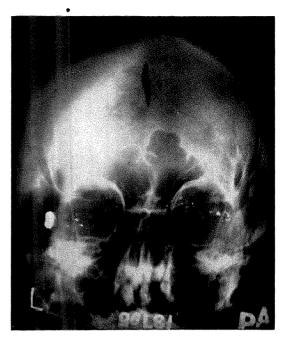


Fig. 2. Case II. Posteroanterior view made with the patient prone. Note the collection of air adjacent to the fair in the midline. The bullet and its path are well known. Lateral views of the head did not demonstrate the pneumocranium.

poste canterior projection, there was a small collection of air in the midline in the region of the falx which was interpreted as a subdural pneurocranium.

On October 22 the patient became more alert. Relatives signed him out of the hospital, and he disappeared.

The mechanism by which air is trapped within the skull in traumatic pneumocranium has been well described by others.<sup>1,2</sup> The mertality in untreated cases is 50 per cent. In the great number of head injuries associated with automobile accidents, this condition must occur more often than hitherto recognized. It should be suspected in all kallfractures in which a serosanguineous cischarge occurs from nose or ears; or in which the fracture extends into the sinuses.

In routine films of the head with the roentgen beam vertically placed, a small amount of subdural air evenly distributed over the cortex might be overlooked. Therefore, when pneumogranium is suspected, it

is necessary to make additional films in the posteroanterior and lateral projections with the roentgen beam horizontal.

#### REFERENCES

1. DANDY, W. E. Pneumocephalus (intracranial pneumatocele or aerocele). Arch. Surg., 1926, 12, 949-982.

- 2. Sm TH, J. S., and MALCOLMSON, P. H. Traumatic pneumocephalus. *Canad. M. Ass. J.*, 1934, 30, 650-651.
- 3. Madigan, J. P. Accidental pneumo-cranium. Virginia Med. Monthly, 1934, 61, 536-537.
- 4. Taft, R. B. Unusual case of traumatic pneumocephalus. Am. J. Roentgenol. & Rad. Therapy, 1931, 25, 800-801.



## THE GASTROINTESTINAL RESPONSE OF AVERAGE, HEALTHY CHILDREN TO TEST MEALS OF BARIUM IN MILK, CREAM, MEAT AND CARBOHYDRATE MEDIA\*

By LAWRENCE REYNOLDS, M.D., ICIE G. MACT, Ph.D., HELEN HUNSCHER, Ph.D., and MART BATES OLSON, M.S.

DETROIT, MICHIGAN

TN A ROENTGENOLOGICAL study of the behavior of the pyloric sphincer it was shown that acid concentration is not the principal factor controlling the opening and closure of the pyloric sphincter in man nor is the initiation of gastric emptying affected by the difference in consistency (viscosity) of various foodstuffs. More recently, quantitative studies have dermonstrated that although hydrochloric acid is an efficient stimulus for the enterogastric reflex, the quantity excreted into the stomach is generally so diluted that after passing through the pylorus there is seldom an effective concentration in the intestine.7 On the other hand, it has been demonstrated that gastric tone and the force of gastric peristalsis may be changed by different stimuli applied in adequate strength to the small or large intestine. Among the conditions within the intestine that affect gastric motor activity are mechanical distention, chemical irritation, the action of hypertonic or hypotonic solutions, and the presence of products of protein and starch digestion. It had been proved that fat 10,12 and carbohydrate23 inhibit gastric secretion and motility through a humoral mechanism whose active principle has been given the name of enterogastrone. Subsequently, experiments on the extract of the duodenal mucosa containing enterogastrone suggest that the e may be two active principles, one which inhibits secretion and another which inhibits motility.10 This mechanism, which affects secretion and motility, whether it be of humoral or nervous nature, or both, no doubt exerts a strong influence in

providing suitable conditions for digestion of the various foodstuffs.

Fat, presumably, modifies gastrointestinal activity through an inhibitory effect on gastric secretion and motility, thus rendering the duodenal contents neutral or only slightly acid.28 Carbohydrates entering the aermal, empty stomach inhibit hunger contractions, and the same phenomenon occurs in the denervated stomach as the result of a humoral factor (not carbohydrate per se) produced by the presence of carbolaydrate in the upper intestine.22 The nhibition persists until the onset of digestive contractions, an interval which is short following ingestion of usual amounts of carbohydrate but which may lengthen to several hours when concentrated solutions are present. Apparently this rescriction is physiologically significant in controlling the rate at which carbohydrate mar enter the duodenum;13 in any event, there is an accumulation of evidence that there is a genuine dissociation betweer the secretory and motor activities of the stomach. 10,19 One of the popular dietary fads today forbids the consumption of carboh drate and proteins at the same meal, the underlying theory based upon the fact that proteins require a high gastric acidity for initial digestion while carbohydrates need an alkaline medium. It has been shown that carbohydrate and protein combined n one meal do not interfere with gastric secretion, and furthermore, that carboaydrate digestion is prolonged and encouraged by mixtures with protein.26

The motility and secretion of the various

<sup>\*</sup> From the Research Laboratory, Children's Fund of Michigan in cooperation with the Department of Boentgenology, Harper Hospital, and the Methodist Children's Village, Detroit.

segments of the alimentary canal are recognized as the prime factors influencing, and influenced by, other processes concerned in the utilization and excretion of foods. Many experimental procedures have been instituted in an effort to determine accurately some of these relationships. The conditions of experiment, in many instances, have prevented any interpretation of the results as those of the natural response. It has been demonstrated that many factors are interrelated in the determination of the response of the alimentary canal: the method of measurement;29,33 the size of the meal ingested; its temperature, consistency and content;29 the nutritional state of the individual; and, the emotional and environmental conditions to which the individual is subject at the time.4 The difficulty in obtaining estimations of the gastrointestinal response of individuals within the range of "normal" has been the inability to obtain measurements upon trained and standardized subjects under adequately controlled conditions which do not interfere with natural response. The difficulties inherent in studies of animals or adults are greatly magnified in attempts toward determining the gastrointestinal responses of children, for consideration must be given to the possible effects of their individual physiological time of progress in growth and possible influences of the growth process itself.

Following the completion of a rigidly controlled metabolic study of average, healthy children over eight consecutive months, roentgenological studies were made of: their gastrointestinal motlity and the variations which may be expected from time to time;17 the effect of carmine upon their gastrointestinal response; and the variation in response due to different types of milks.25 During the metabolic study of chemical growth, the gastroir testinal motility of the subjects was studied by means of carmine markers given every fifth morning to demarcate the fecal unit of each balance period, and by the records of the frequency and wet and dry weights of their defecations over 225 consecutive days. 20 The gastrointestinal response of the same subjects to five different types of test meals is reported in this paper.

The subjects of the studies were carefully chosen as representative of average, healthy children from their medical histories and the results of thorough clinical and laboratory examinations.\* The children were within normal limits in bone and structural development and mentality.† Throughout the study the children, between four and one-half and eight years of age, were subject to the same highly standardized conditions of adequate diet, routine and environment favorable to growth and development which had been maintained during the metabolic investigations.‡

#### EXPERIMENTAL PROCEDURE

Series of roentgenograms were made showing the gastrointestinal tracts of the subjects at frequent intervals following ingestion of test meals composed of barium in five different types of media. An interval of at least one week elarsed between any two series with the same child. The liquid meals were given at body temperature, the solid one at room temperature. The liquid meals all consisted of 2 ounces of barium sulfate in 4 ounces of medium. Water was used as one carrier, providing an inert meal. Meals of different fat content were procured by using 4 ounces of milk (3.5 per cent fat) and 4 ounces of cream (20 per cent fat) as media for the barium. A carbohydrate meal was formed with the barium in 3 ounces of water and I ounce of corn syrup (approximately 30 per cent glucose, 61 per cent carbohydrate). A prozein test meal was composed of 40 grams of bar um sulfate mixed with 100 grams of raw ground lean meat, baked twenty to thirty mirutes and ingested with 200 cc. of water. Based on the total weights of the meals at the

\* Marsh W. Poole, M.D., pediatrician for the Methodist Children's Village, made frequent examinations of the children.

<sup>†</sup> The late T. Wingate Todd, M.D., and C. C. Francis, M. D., Western Reserve University, Cleveland, evaluated the roentgenograms of the subjects and estimated their skeletal ages. The Children's Center, Child Guidance Division of the Children's Funl of Michigan, made the psychological tests.

<sup>‡</sup> The results of the integrated program of investigation of the chemical growth of average, healthy children forms the material for a monograph upon that subject, now being prepared.

times they were ingested, the milk meal had a concentration of 2.33 per cent fat; the cream meal, 13.33 per cent fat; one meal had a concentration of 10 per cent carbohydrate; and the meat meal was approximately 3.5 per cent fat and 7 per cent protein.\*

All meals were ingested in a few minutes except the meat loaf, for which one-half hour was allowed. The children's routine was interfered with as little as possible. No laxatives were given or any alteration made in the diets preceding the studies. The barium meals were given in the morning and were the only food ingested between the evening meal preceding and the completion of the first day's roentgenograms.

After ingestion of the first meal given (water), a roentgenoscopic examination was made (L.R.) to eliminate the possibility of any abnormality in the chest, in the movement of either leaf of the diaphragm, or in the rate or rhythm of the heart. The first exposure in each series was made within twelve minutes after the meal was ingested and additional films were exposed at thirty minute or hourly intervals up to about five hours, in the case of the faster meals, and seven hours in the cases of the slower ones. Throughout the period of observation at frequent intervals (four to eight hours) the subjects were allowed the freedom of a room in which they played; however, they were under strict surveillance at all times to preclade ingestion of food or water. Additional roemtgenograms were procured twenty-four, forty-eight, and in a few instances seventy-two hours, approximately, after ingestion of the meals.

The roentgen examinations were made with the subjects in prone position with the rarget 31 inches from the film and centered on the first to second lumbar vertebra; exposure was  $\frac{1}{5}$  sec. at 92 kv. (peak) and 50 ma. with Potter-Bucky diaphragm. Patterson par-speed screens were used with the smaller children and speed screens with the larger ones. To eliminate some of the obvious difficulties in comparison or evaluation, each roentgenogram was photographed and reduced to a  $1\frac{1}{2}$  by  $2\frac{1}{2}$  inch reproduction. Each series of prints was then mounted upon a cardboard strip, making direct and comparative estimations possible.

#### RESULTS

Of the roentgenograms made in this study of the variations in the motility of the different segments of the gastrointestinal trace of enildren, the reproductions of the expesures illustrative of the five barium meas (water, glucose, milk, cream and meat) in 4 subjects at comparative time intervals are presented in Figures 1-7. All of the zeries of roentgenograms show the same wide range of individual variation which characterized the subjects during the previous study over eight continuous months and the physiological pattern described in the preceding report. IT Variations in the size, shape, and position of the stomachs of all subjects filled with the same amount of mea are apparent but no anomalies are portraved.

Emptying Time of the Stomach. In Table 1 are given the physical data and the gastric emptying times for the different individuals in the 33 series of observations made. The inert water meal emptied from the stor acha (average 1.9 hours) appreciably faster than any of the other meals. The average emptying times for the milk and glucose meals were 3.1 and 3.3 hours, respectively, and for the meat and cream meals 5.0 and 4.8 hours, respectively. It is evident that the type of vehicle or conveyer of the barium has a specific motor effect upon the egression of the meal through the pylerus, findings which substantiate those of Johnston and Ravdin<sup>13</sup> and Gershon-Cohen and Shay.8

The products of carbohydrate,<sup>23</sup> fat<sup>13,22</sup> and protein<sup>9,31</sup> digestion are known to have a physiclegical significance in controlling the rate at which these substances enter the cuocenum, whether through a humoral or nervous action or both on the pyloric reflex mechanism by way of the small intestine. In the present series of observations the water meal began to leave the stomach immediately following its ingestion and within ten minutes a considerable amount of barium mixture had entered the jejural pops (Fig. 1). With the water-

<sup>\*</sup> During cooking the water lost was approximately 30 grams. The resulting meat loaf contained, roughly, 10 grams of fat and 20 grams of protein, providing concentrations in the total 290 grams of the meal of approximately 3.5 per cent fat and 7 per cent protein.

barium meal the stomach exhibited a normal two-wave type of peristalsis. There was no pylorospasm and no abnormality in the orderly egress of the meal, the stomachs completely emptying their barium content within 2.8 hours (average 1.9 hours), and the barium distributing throughout the small gut as shown in detail in the accompanying illustrations. On the contrary, the carbohydrate-barium meal

increase in volume of gastric contents and a decrease in their concentration. Ravdin, Johnston and Morrison<sup>24</sup> found that though <sup>215</sup> cc. of glucose solution was the maximum amount of fluid introduced into the stomach, more than 500 cc. were removed at the end of an hour, the additional water having been drawn into the stomach as a diluent for the sugar solution. Concentrations of glucose varying from 3.5 to 50.0

Table I

PHYSICAL DATA AND GASTRIC EMPTYING TIME: WITH DIFFERENT TYPE FOODS

Subject	Sex	Age	Recumbent Length	Weight	Physical Type*	Gastric Emptying Times†				Average Num- ber Defeca- tions During	
						Water	Milk	Meat	Cream	Carbo- hydrate	8 Months' Metabolic Study
V		mo.	cm.	kg.		hr.	hr.	hr.	hr.	hr.	per day
D.P.	$\mathbf{M}$	117	143.5	34.05	0.0226	1.0	3.0	3.5	2.5	3.0	1.2
W.P.	$\mathbf{M}$	113	126.2	27.78	6.0240	2.0	3.0	4.5	5.5	3.0	1.6
H.H.	M	102	129.7	26.56	0.0230	2.0	1.5	and the state of t			1.6
P.W.	$\mathbf{F}$	98	127.8	25.51	0.0231	1.5		7.0	page and a second	Au	1.0
F.C.	M	• 96	128.0	26.79	0.0234	1.8	4.0	3.0	6.5	3.0	1.4
R.S.	$\mathbf{M}$	88	123.7	22.36	0.0228	2.8	2.5	7.0	4.5	4.0	2.4
B.F.	$\mathbf{F}$	86	117.6	21.68	0.0237	1.5			• •	3.5	1.6
B.M.	$\mathbf{F}$	81	114.7	19.07	0.0234	2.5	4.5	6.0	-		1.7
J.H.	M	74	117.4	21.91	0.0238	1.3	3.0	5.0		3.0	1.8
Mean				1.9	3.1	5.0	4.8	3.3	1.6		

<sup>\* (</sup>Cube root weight) divided by recumbent length.

(10 per cent) retarded the gastric motility to a maximum of four hours (average 3.3 hours). These results are in agreement with recent experimental work on gastric physiology in man<sup>8,13,19,24</sup> involving the influence of osmotic pressure change produced by sugar solutions on pyloric action and suggest that osmotic pressure above or below isotonicity definitely influences pyloric action and gastric evacuation, and the greater the hypertonicity of the test meal, the slower the gastric emptying.

It has been found that the body, which is organized for physiological homeostasis,<sup>2</sup> always attempts to bring the ingested fluid to the isotonic state; consequently, when a hypertonic solution is introduced into the stomach there follows a rapid

mg. per 100 cc. were given and after an hour the concentrations of glucose in the small intestine only varied from 2.6 to 5.3 mg. per 100 cc., irrespective of concentration given.

Gershon-Cohen and Shay<sup>8</sup> conclude that "the pyloric action was motivated locally through duodenal stimulation by chemical action, and that this same mechanism is influenced by physical stimuli as represented by changes in osmotic pressure away from isotonicity. Gastric emptying time alone cannot be used as an index of pyloric function when considering osmotic tens on of agents given by mouth because of the migration of fluid which takes place through the stomach wall when the test meals are not isotonic."

<sup>†</sup> Times given are from completion of ingestion of test meals.

Consideration of the physiological homeostatic effect of the stomach in rendering an ingested hypertonic fluid isotonic makes very valuable a comparison of the changes in the volume of the stomach contents of the same individual when inert and hopertonic substances are used as conveyers of the barium. Although it is recognized that planimeter measurements of the rcentgenograms, representing the square centimeter area of the maximum longitudinal section of the stomach containing these different barium meals, has its limitations so far as exactness is concerned (the third dimension cannot be obtained30) yet qualitative information significant to the recentgenologist can be secured (Table 11). From the measurements of the barium shacows of the stomachs when filled with equal quantities of the inert water-barium mixture and the slightly hypertonic carbohydrate-barium meal it is obvious that there are variations in the stomach size of the different subjects and that even by the time the first film could be taken, the carbohydrate meal caused a significant increase in size of the stomachs.

The increases in the average differences between the size of the stomachs with the water and carbohydrate meals after forty and seventy-five minutes (Table II) era shasize the length of time devoted to rapid dilution of the sugar mixture. Inspection of Figures 2 and 3 accentuates the fact that while little progress is made in the emptying of the carbohydrate mixture from the stomach, a quantity of barium carrier, equal or greater than with water meal has been emitted into the small intestine by the end of seventy-five minutes. It would seem that the intestinal response to the carbohydrate meal involves not only the original 6 ounce meal but also ar increase of several times that volume.

If the sizes of the stomachs (Table II) are stated in terms of per cent of their measurement twelve minutes after the water meal (assuming the size twelve minutes after ingestion of the water meal to be 100 per cent) the average increase in

size cue substitution of the sugar for water is all per cent. At the three intervals (Talde II) the average sizes of the stomachs were: with the water meal after twelve minutes, 100 per cent; after forty minutes, 72 per cent; and after seventy-five minutes, 63 per cent; with the glucose meal after twelve minutes, 128 per cent; after forty

TABLE II

INFLUENCE OF HYPERTONIC CARBOHYDRATE SOLU-TION\* UNGE THE SIZE OF THE BARIUM SHADOW OF THE STOMACH AS MEASURED BY THE PLANIMETER T

Child	Barium Me-	Surface Area of the Stomach after Ingestion of Barium Meal					
		12 min.	40 min.	75 min.			
AMMONDA SALIKA - POPULINA		attackenses og er er en	(sq. cm.)				
D.P.	Water Ca∄xohydrate	60 85	‡ ‡	‡ ‡ ‡			
W.P.	Water Castohydrate	66 83	52 86	42 82			
F.C.	Wæer Ca⊯bohydrate	76 99	53 92	48 87			
R.S.	Warer Camphydrate	8 <u>5</u> 107	60 104	52 97			
B.F.	Wažer Cas∷chydrate	83 94	57 96	† † †			
J.H.	Wazer Camuhydrate	65 84	† ; ;	† † ‡			
	Azerage difference	e 2©	39	41			

<sup>\*</sup> Cora syru: Lised in the carbohydrate-barium mixture produced a soncesseration of 10 per cent carbohydrate.

minutes, \*22 per cent; and after seventy-five minutes, 117 per cent. While the size of the stomach increased rapidly and then decreased much more slowly with the sugar meal, it remained larger after seventy-five minutes than with the water meal after twelve minutes.

These solution does cause an increase

<sup>†</sup> The planimeter used was a disc planimeter made by G. Coradi, Zurich.

<sup>‡</sup> Complete annach not shown on both films precluded measurement.

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in the volume of the gastric contents.<sup>24</sup> Moreover, they explain the satiety and sense of fullness followed by a cessation of hunger contraction and a submerging of appetite which follow the consumption of candy or sweets at any time.

A study of the protocols of the milkbarium meal shows that there was an initial delay in the passage of this meal through the pylorus into the small gut, producing an average gastric emptying time (Table 1) of 3.1 hours in contrast to 1.9 hours with the water barium meal. Twelve minutes following ingestion of the milk meal the stomachs of 8 subjects still retained all of the milk-barium mixture. Moreover, the first films exposed (Fig. 1) show the presence of only one peristaltic wave in the stomachs. The second films (Fig. 2), exposed thirty minutes later, show an orderly two-wave type of peristalsis in the stomachs and some of the barium mixture in the distal jejunal loops. The subsequent films exposed (Figs. 3-7) show an orderly emptying of the gastric content and the normal passage through the small gut, the small intestine pattern being somewhat at variance with that shown in the barium-water meal series. These results are in agreement with those of Gershon-Cohen and Shay<sup>9</sup> who found that during the early stages of milk digestion, the milk-barium meal passed through the pyloric sphincter into the duodenum as each and every antral peristaltic wave approached the orifice and, once some of the mixture had passed into the duodenum after the initial gastric delay, there seemed to be a perfectly orderly peristalsis and an orderly evacuation of the gastric content.

The cream-barium meal, containing approximately 13 per cent fat, required an average of 4.8 hours to empty from the stomach, in contrast to 1.9 hours and 3.1 hours for the water-barium and milk-barium (2.33 per cent fat) meals, respectively (Table 1), verifying the observation that the intensity of the control of the pyloric action is proportionate to the fat content. In a study of the gastric evacua-

tion of adult subjects, Gershon-Cohen and Shay<sup>a</sup> found, roentgenologically, that during the early stages of milk digestion the pylorus appeared to be closed and even spastically contracted with the cream meal, the spasm of the pylorus being so marked that it reflected backward into the antrum and forward into the cap so that all the stomach contracted simultaneously.

The fact that cream causes a retardation in the egress of the meal from the stomach and thereby affects the rate of availability of orally ingested carbohydrate has recently been put into practical use in the care of diabetic patients treated with injections of protamine zinc insulin;21 for example, a combination of bananas and cream, which produces a slowed gastrointestinal rate, delaying the time of maximum absorption from one to two hours, prevents an overloading of blood sugar and eliminates the precipitous drop in blood sugar concentration produced by carbohydrate alone. Since the activity of the protamine zinc insulin is not manifested for several hours after its injection, the importance of delaying the post-prandial rise in blood sugar by means of sustained absorption is obvious. This delay caused by a fat mixture such as bananas and cream allows the absorptive period to come within the range of insulin activity of the current injection.

The protein meal composed of the baked meat loaf accompanied by water had a different volume and consistency than the other barium meals studied,\* and the time required for its ingestion ranged up to thirty minutes. The average gastric emptying time was 5.0 hours as compared with 1.9 hours with the water-barium meal. It is known that protein requires a high gastric acidity for initial digestion; consequently, interest has been centered upon a study of the hydrochloric acid present in the acid chyme and the subsequent pH of the duodenal content upon gastric peristalsis and

<sup>\*</sup> During cooking the water lost was approximately 50 grams. The resulting meat loaf contained, roughly, 10 grams of fat and 20 grams of protein, providing concentrations in the total 290 grams of the meal of approximately 5.5 per cent fat and 7 per cent protein.

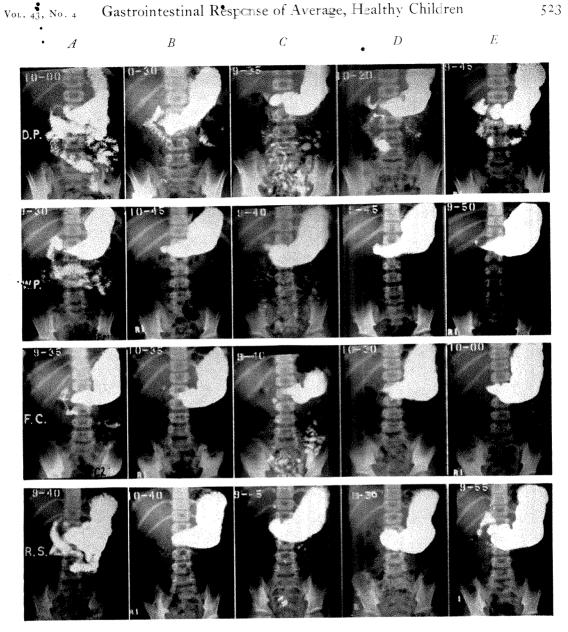


Fig. 1. Twelve minutes after ingestion: I, water meal; B, milk meal; C, meat meal; D, cream meal; £ carbohydrate real.

evacuation. Here again the body demonstrates homeostasis to a significant degree, for the excellent investigations of Mann and Bollman and their collaborators 18 Fave shown that the stomach and duodenum have remarkable power of compensating for marked alterations in their secresory mechanisms. There is an increased acidity of the duodenal content following a protein meal but the normal duodenum has the

ability to neutralize the acids from the stomach that reach it, thus permitting an almost unvarying reaction to their content by the je unum and ileum. It was shown by this group of investigators that, in dogs, after a meal of 100 grams of meat the reaction of the duodenal content during the next hour or two fluctuated within the range of pH 6.4 to 3.5 after which there was a gradual tendency towards neu-

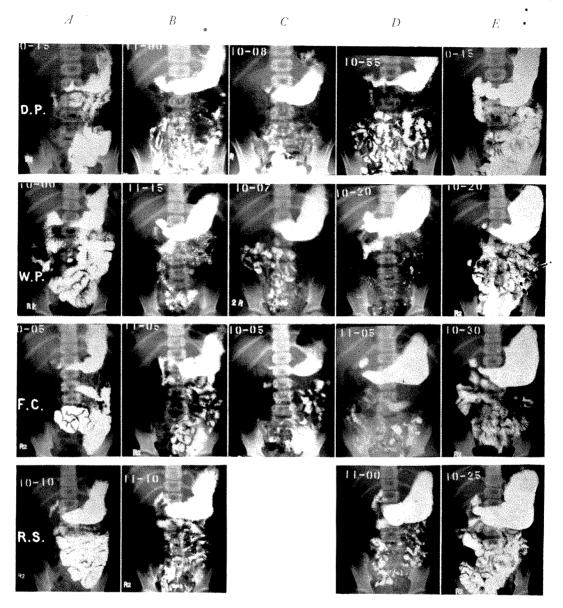


Fig. 2. Forty minutes after ingestion: A, water meal, B, milk meal; C, meat meal; D, cream meal, E, carbohydrate meal.

trality. Following a carbohydrate meal, the reaction ranged from pH 6.3 to 4.3 and after a fat meal from pH 6.8 to 5.8. The acidity of the duodenum after meals appears to depend largely on the rate and amount of acid formation in the stomach (results which are in agreement with other investigators), the meals modifying the gastric acidity through an inhibitory effect on gastric secretion and motil ty and the

variation in acidity compensated in the duodenum in such a manner as to render the content neutral or slightly acid.

Enptying Time of the Intestines. Our knowledge of the mechanics of the small intestine is still incomplete. From the experimentation thus far carried out, it would seem to be chiefly the action of the muscularis mucosae that keeps the food finely divided so that the digestive juices may

operate as well as act in some manner in the propulsion of the food along the course of the small intestine.

It has long been known that peristaltic waves are visible in the small intestine only when it is somewhat overloaded with a mass of food, though the jejunal and ileal patterns are quite distinct in their appearance. When the food approaches the region of the ileocecal valve, the intestinal move-

ments are much less active and there is considerable massing and overlapping of the shadows and the outline of the intestine n that region is less well defined. The nearer the food approaches the end of the small in estine the less the peristals is visible. During roentgenoscopic observations (L.R.) a sudden propulsion of the contents of the last few inches of the ileum into the secum is frequently seen, and this

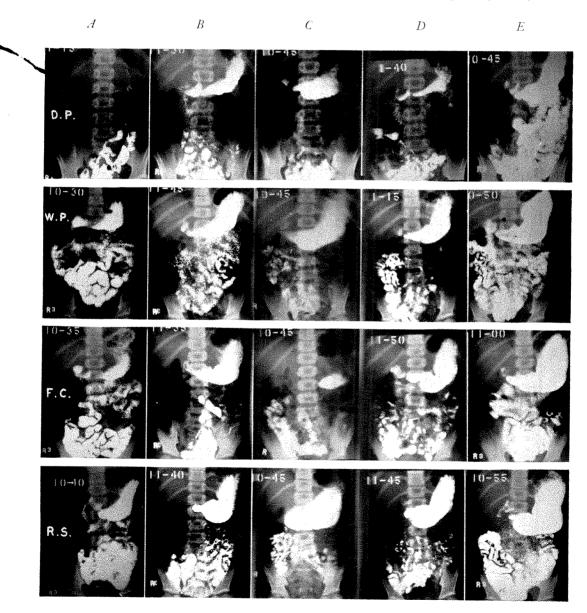
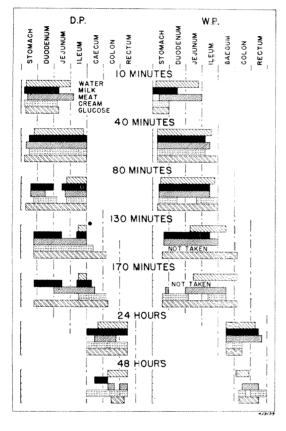


Fig. 3. Seventy-five minutes after ingestion: A, water meal; B, milk meal; C, meat meal; D, cream meal; E, carbably date meal.

occurs with such suddenness that it leaves us somewhat bewildered as to the exact mechanism which brought it about—whether it is the result of a sudden spasm that "synchronized with the opening of the valve," as suggested by Barclay, or some other mechanism of physiologic propulsion is not clear-cut enough to determine.

the reproductions are arranged so that comparisons of the differences of reaction to different meals in the same child may be illustrated. The widest range of individual difference is represented by these 4 children and all observations made from their roent-genograms represent the group adequately. Each child has a definite response typical of the individual while at the same time



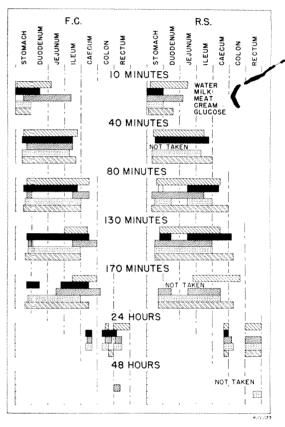


CHART I

CHART H

Under normal conditions there is no absorption of carbohydrate, fat or protein from the stomach.<sup>3,33</sup> The real region of absorption is the small intestine. These substances are generally digested and absorbed by the time the chyme reaches the ileum. If any undigested food enters the large intestine, however, it may be absorbed there.

In the series of roentgenograms for the children who received all of the test meals,

each child shows a greater variation in response to the different meals, results which are in agreement with those of Ladd with infants. Consistently, the most rapid motility is shown by the water meal and the least by the meat and cream meals. To clarify and bring the clinical estimations together more closely the relative motility of the 4 children in response to the five different meals has been represented in Charts I and II. An inspection of the charts

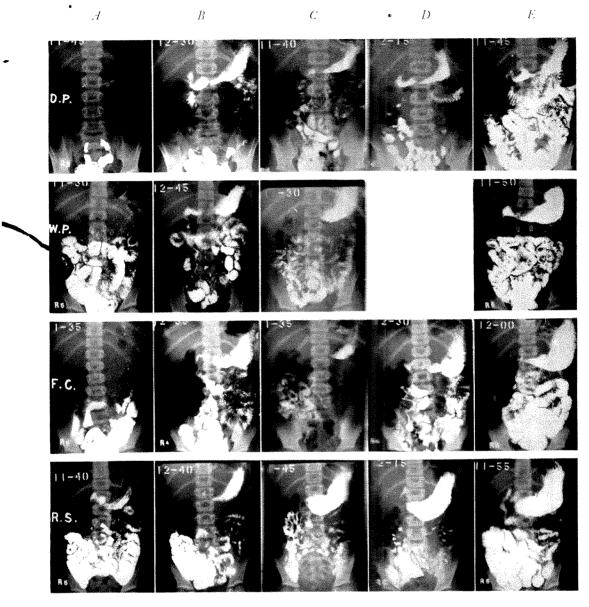


Fig. 4. One hundred and thirty minutes after ingestion: A, water meal; B, milk meal; C, meat meal; D cream meal; E, carbohadrete meal.

seems to indicate that the children with the most rapid gastric motility have the least rapid intestinal motility, and the children with the least rapid gastric motility have the most rapid intestinal motility.

The initial roentgenograms (Fig. 1) portray the logical intestinal response consequent to the reactions of the stomachs to the various types of the test media. Due to the gastric inhibition only one of the chil-

dren (J.F.) emitted some of the milk and cream meals into the jejunum during the first twelve minutes after ingestion. The same child and one other (R.S.) show some of the carbohydrate meal in the jejunum after the same interval. The typical, regular progress of the water meals is apparent. Although the protein meal had advanced farther into the tract twelve minutes after complet on of ingestion of the meal, the

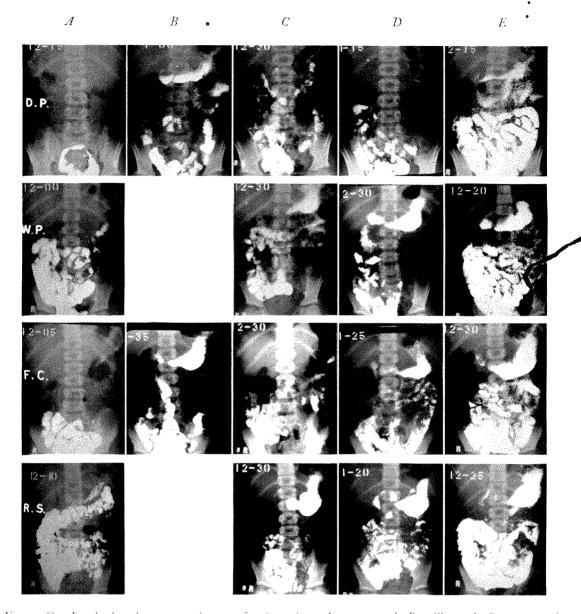


Fig. 5. One hundred and seventy minutes after ingestion: J, water meal; B, milk meal; C, meat meal; D, cream meal; E, carbohy trate meal.

longer time allowed for consumption of the unappetizing mixture undoubtedly contributed to the result shown.

After forty minutes (Fig. 2) the water meal of each of the subjects was somewhat massed in the terminal ileac loops; the stomachs were half empty or more; and the rugae were clearly outlined. The leading portions of the milk meals had progressed approximately as much as the water meals but in not as great quantity and the roent-

genograms show an entirely different pattern. The meat meals showed the individual pattern indicated on the initial exposures but in a greater concentration. The cream meals had advanced as far as the ileum in all cases but wider individual variations were shown with this meal and less of the material was emptied from the stomach than with any of the other meals. For all the subjects the glucose meals indicated a much greater dispersion of the barium in the duodenum, jejunum and ileum, perhaps due to the large addition to the volume of liquid in which the barium was distributed. The pattern of the glucose mixture was more like that of the water meal than any of the others.

Approximately seventy-five minutes after ingestion (Fig. 3) the water meaks had made consistent progress, and the morility shown for the different children was at the

same reactive rate for each. The milk meals also showed continuous progress although appearer by there was a cessation or slowing down in the emission of stomach content for all of the children except W.P. This inhibition is even more pronounced with the mean meals, with which practically all gastric emprying seems to be stopped at this interval, with a tendency for the meal to accumulate in the lower ileum and cecum,

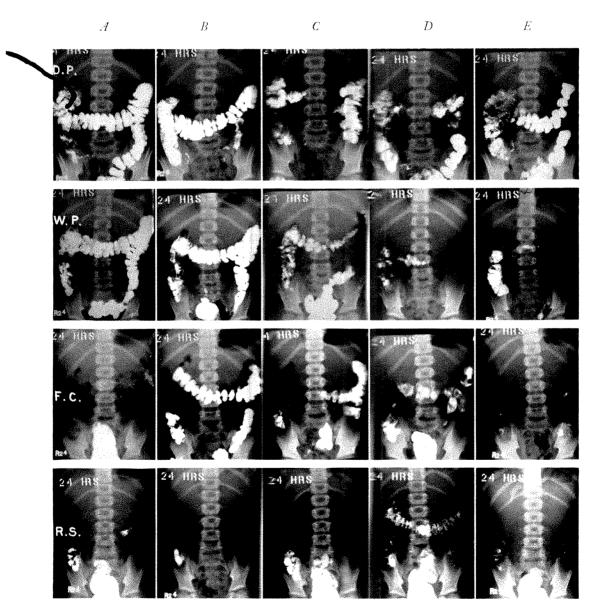


Fig. 6. Twenty-four hours after immestion: A, water then; B, milk meal; C, meat meal; D, cream theal; E, carbonyain the meal.

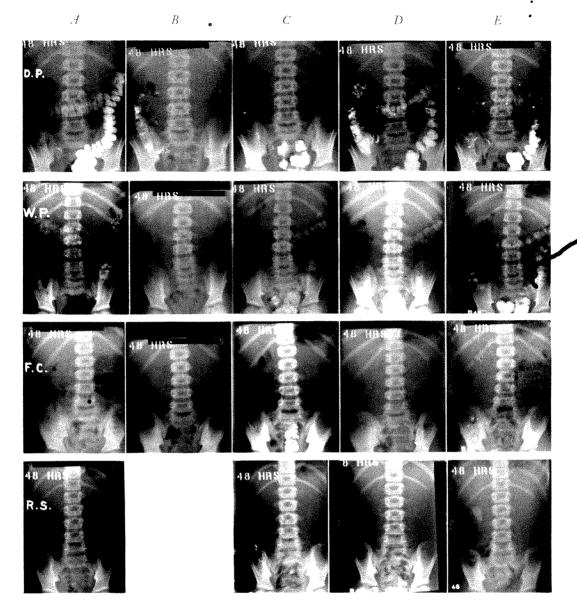


Fig. 7. Forty-eight hours after ingestion: A, water meal; B, milk meal; C, meat meal; D, cream meal; E, carbohycrate meal.

leaving the jejunum entirely empty. The same effect was quite pronounced with the cream meals which accumulated in masses of greater density than those of the meat. After this interval the glucose meals were much more widely diffused throughout the entire length of the small intestine

In Figures 4 and 5 the progress of the different meals is consistent with the indications of the preceding exposures. In these illustrations the roentgenograms of

the 4 children illustrate clearly the enormous increase in quantity of the glucose meal; the rapid, orderly progress of the water meal; and the inhibitory gastric effect produced by the milk and cream meals. The individuality of each child's response is emphasized by the roentgenograms of D.P. and R.S. after 130 minutes (Fig. 4).

The twenty-four and forty-eight hour reproductions (Figs. 6 and 7) indicate all the meals in the cecum, colon, or rectum

twenty-four hours after ingestion. No consistent variations may be seen in the response to different meals; individual response is quite obvious. These alterations in the response would be expected, due to the fact that in the large intestine the material has been digested and fecal formation and motility are dependent upon additional physiologic influences more than upon the source of the material.

#### SUMMARY

The gastrointestinal response of healthy children to test meals of barium in water. milk, cream, meat and carbohydrate media was determined roentgenologically as one of many coordinated studies designed to present a more complete evaluation of the processes involved in chemical growth. The gastrointestinal investigations were made following eight months of intensive metabolic study of the same children, who had been selected by thorough physical and mental examinations as representative of average, healthy children. The subjects lived in an adequate "home" environment and their habits of diet and elimination were well standardized.

The different test meals were studied at least one week apart and were ingested in the morning into a food-empty smomach. Roentgenograms were exposed immediately after administration of the meals and each half hour or hour thereafter until the stomachs were empty. During this interval (four to eight hours) the children played indoors but were restrained from regesting any other food or liquid. Additional roentgenograms were obtained twenty-four, forty-eight, and, when necessary, seventytwo hours after the initial examination. The 300 exposures procured clearly Mustrate variations: among individuals' responses to the same meal; in the individual's responses to different meals; and in the responses of the different sections of the tract.

The water meals produced the most consistent and constant reactions within both stomachs and intestines. The milk cream, and carbohydrate meals were all subject to

an initial delay in gastric emptying. In comparison with the progress of the water meals through the intestine, the milk mixtures were slightly delayed and the cream meal considerably retarded. The meat meals, containing both protein (7 per cent) and faz (3.5 per cent), did not produce the same delay in gastric emptying shown by the cream meal and made more rapid progress through the small intestine until the leading portions reached the terminal ileac loops. At this time the protein-fat mixtures seemed to exert a stronger gastric inhibition than did the cream media. Following the initial delay in gastric emptying the carbohadrate meal filled the entire small intestime very rapidly and at the same time the samach increased in size, indicating the exceme rapidity of action of a humoral mechanism which reacts to bring stomach contents to isotonicity by osmotic induction of water into it.

#### REFERENCES

- I BAZZLAY, A. E. The Digestive Tract. Cambridge Wniversity Press, London, 1933.
- 2: CASSON, W. B. Organization for physiological mereostasis. *Physiol. Rev.*, 1929, 9, 399-431.
- 3 Carron, W. B. The Mechanical Factors of Egestion. International Medical Monograph. Edward Arnold & Co., London, 1911.
- 4. CANON, W. B. Bodily Changes in Pain, Hunger, Sear and Rage. Second edition. D. Appleton Co. New York, 1929.
- 5 Самьон, А. J., and Johnson, V. The Maerinery of the Body. University of Chicago Eress, 1937.
- E. CRODER, J. O., and THOMAS, J. E. A further smally of inhibitory effect on gastric peristalsis of the products of protein digestion. Am. J. Physiol., 1938, 123, 44.
- The mas, J. E. Editorial. The regulation of gastic emptying. Am. J. Digest. Dis., 1938, 5,
- E. GERSHON-COHEN, J., and SHAY, H. Effect of composition of changes in small intestine upon gastric maptying in man. Am. J. Digest. Dis. & n'rition, 1937, 4, 637-643.
- E. Gers-ion-Cohen, L., and Shay, H. Experimental studies on gastric physiology in man.

  II. A study of pyloric control. The rôle of mik and cream in the normal and in subjects with quiescent duodenal ulcer. Am. J. Roentmerol. & Rad. Therapy, 1937, 38, 427-446.

- Gray, J. S., Wieczorowski, E., and Ivy, A. C.
   Inhibition of gastric secretion by extracts of normal male wrine. Science, 1939, 86, 489-490.
- 11. HOERNER, M. T. Effect of exclusion of pancreatic secretion by evulsion of pancreatic ducts on reaction of duodenal content. Am. J. Digest. Dis. & Nutrition, 1935, 2, 295-297.
  - Hoerner, M. T. Effect of exclusion of pancreatic secretion by a pancreatic fistula on reaction of gastric, duodenal and jejunal contents. Am. J. Digest. Dis. & Nutrition, 1935, 2, 298-300.
- 12. IVY, A. C., and FARRELL, J. Studies on motility of transplanted gastric pouch. Am. J. Physiol., 1926, 76, 227.
- 13. Johnston, C. G., and Ravdin, I. S. Action of glucose on emptying of stomach effect of varying concentrations in both normal stomachs and after various gastric operations. Ann. Surg., 1935, 101, 500-505.
- 14. LADD, M. Influence of variations of diet on gastric motility in infants. Tr. Am. Pediat. Soc., 1913, 25, 74.
- 15. McClure, C. W., Reynolds, L., and Schwartz, C. O. On the behavior of pyloric sphincter in normal man. Arch. Int. Med., 1929, 26, 410.
- Macy, I. G., Reynolds, L., and Soubers, H. J. Effect of carmine upon gastrointestinal motility of children. Am. J. Physiol., 1939, 126, 75-81.
- 17. Macy, I. G., Reynolds, L., Souders, H. J., and Olson, M. B. Normal variation in gastro-intestinal response of healthy children. Am. J. Roentgenol. & Rad. Therapy, March, 1940, 43, 394-493.
- 18. Mann, F. C., and Bollman, J. L. Symposium concerned with duodenal factors in neutralization of acid chyme. *Am. J. Digest. Dis. & Nutrition*, 1935, 2, 284–285.
- 19. Manville, I. A., and Munroe, W. R. Studies on gastric hunger mechanism. II. Inhibitory effect of dextrose solutions. Am. J. Digest. Dis. & Nutrition, 1937, 4, 561-573.
- Olson, M. B., and Macy, I. G. Relationship of gastrointestinal motility of growing children to fecal formation and excretion of food elements. To be published.
- 21. Pollack, H., and Dolger, H. Effect of fat on rate of availability of orally ingested carbohydrate. *Proc. Soc. Exper. Biol. & Med.*, 1938, 39, 239-242.

- 22. Quicley, J. P., and Phelps, K. R. Mechanism of gastric motor inhibition from ingested carbonydrates. *Am. J. Physiol.*, 1934, 109, 133-133.
- 23. QUICLEY, J. P., ZETTLEMAN, H. J., and IVY, A. C. Ar alysis of factors involved in gastric motor inhibition by fats. Am. J. Physiol., 1934, 108, 643-651.
- 24. RAVDIN, I. S., JOHNSTON, C. G., and MORRISON, P. J. Comparison of concentration of glucose in stomach and intestine after intragastric administration. *Proc. Soc. Exper. Biol. & Med.*, 1933, 30, 955-958.
- REYNOLDS, L., MACY, I. G., and SOUDERS, H. J.
  Gastrointestinal response of children to test
  meals of barium and pasteurized, evaporated,
  and base-exchanged milks. J. Pediat., 1939,
  15, 1-12.
- 26. Sha<sup>+</sup>, H., Gershon-Cohen, J., and Fels, S. S. Is gastric secretion or digestion impaired by a mixture of carbohydrate and protein in the di≥t? Am. J. Digest. Dis. & Nutrition, 1936, 3, 235-238.
- 27. TELPER, S. V. Studies in calcium and phosphorus metabolism. Part 3. Absorption of calcium and phosphorus and their fixation in the skeleton. Quart. J. Med., 1923, 17, 245.
- 28. Thomas, J. E., and Crider, J. O. Effect of fat or the pH of contents of duodenum. Am. J. Physiol., 1936, 114, 603-608.
- 29. Todo, T. W. Behavior Patterns of the Alimentary Tract. Williams & Wilkins Co., Baltimore, 1930.
- 30. Todo, T. W., and Kuenzel, W. Studies in the all mentary tract of man. 1. Attainment of reliability in gastric responses. J. Lab. & Clin. Med., 1929, 14, 1017-1032.
- 31. VAN LIERE, E. J., and SLEETH, C. K. Studies in gastric motility; relation of size of the meal to gastric emptying time in the dog, using a meal rich in fat and protein. Am. J. Digest. Dis., 1938, 5, 18-19.
- 32. Van Liere, E. J., Sleeth, C. K., and Northup, D Relation of size of the meal to emptying time of human stomach. *Am. J. Physiol.*, 1637, 110, 480-482.
- Verzar, F., and McDougall, E. J. Absorption from the Intestine. Longmans, Green & Co., Ltd., London, 1936.



## 'EFFECT OF INJECTIONS OF DISTILLED WATER ON THE GROWTH OF IRRADIATED MOUSE SARCOMA 180\*

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IN A PREVIOUS communication, 4 it was shown that tumor transplants of mouse sarcoma 180 when irradiated in vivo showed no regression with a dose of less than 500 roentgens, and very few with less than 750 r. With a dose of 1,000 r, about 50 per cent of the cases showed regression. With a dose of 1,500 r, about 85 per cent of cases showed complete regression, but with a dose greater than 1,800 r, tumor regression occurred in 100 per cent of the cases.

If tumors are treated with 1,500 r while in the host, and immediately removed and implanted into normal mice, about 30 per cent will grow progressively as in the case of tumor fragments irradiated in vitro with the same dose of roentgen rays. If they are allowed to remain in the original host for twenty-four hours before reimplantation, only 50 per cent will take while if left three days before re-implantation, only 20 per cent will result in takes. In order to get complete inhibition of growth it is necessary to leave the tumor in the animal for six days or longer.

Chambers and Grand, and Sugiura and Cohen, using the tissue culture technique, recently reported additional information concerning the viability of irradiated tumor tissue. Tumors (mouse sarcoma 180) rradiated in vivo with a dose of 1,500 r and then removed within twenty-four hours and cultured, generally will grow progressively in culture in all cases. If the irradiated tumors are allowed to remain in the original hosts for three days before culturing, only about 33 per cent will show slight migration and growth of sarcoma cells. On the other hand, complete inhibition of sarcoma growth will occur in those left in the

original animals for five days or longer.

The pariations in the viability of tumor fragments at different intervals after irradiation can be correlated with changes in their histological appearance. Tumors remaining seventy-two hours in the host after irradiation with 1,500 r show markedly swolen cells. The volume of these swellen cells is approximately twelve times that of the normal tumor cells (Fig. 1). Experimental evidence has indicated that the swelling of tumor cells is not a postmorter change. Therefore, it is our belief that the death of the tumor cells may be due to swelling.

Recently Failla<sup>2</sup> advanced the "fluid heory concerning the biological action of radiation. According to Failla, roentoen rays tend to increase the number of electrolytic ions in the cytoplasm of irradated tumor cells. Such a change would custurb the osmotic equilibrium and available fluids would tend to enter through the semipermeable cell membrane to equalize the ion concentration on both sides of the membrane. Swelling generally follows, which, if sufficient, disrupts the cell. Falla suggested that the lethal effect of menteen rays is due possibly to an initial swelling and consequent dilution of the cytoplasm which interferes with the norma physiological processes. According to this theory it should be possible to increase the radiosensitivity of a tissue by increasing its circulation or by decreasing the osmotic pressure of the surrounding extracellular fluids. This can be done by injecting water into the tumor following irradiation. The following experiments were carried out with the object of testing this supposition.3

<sup>\*</sup> Presented before the Third International Cancer Congress, Atlantic City, N. J., Sept. 11-15, 1939.



Effect of Water upon the Growth of Nonirradiated Mouse Sarcoma 180. As a preliminary study, we determined the extent of the deleterious action of distilled water upon the development of transplanted tumors (mouse sarcoma 180) in mice. This was done because the results of our in vitro experiments<sup>7</sup> showed that the growth caat 4-5°C. grew normally when implanted into mice.<sup>8</sup> The pH of ordinary distilled water is generally 5.5.

Subsutaneous inoculations of tumor tissues into healthy young adult mice (Bagg albino mice and Rockland albino mice), usually weighing from 22 to 25 gm., were carried out by the usual trocar method.

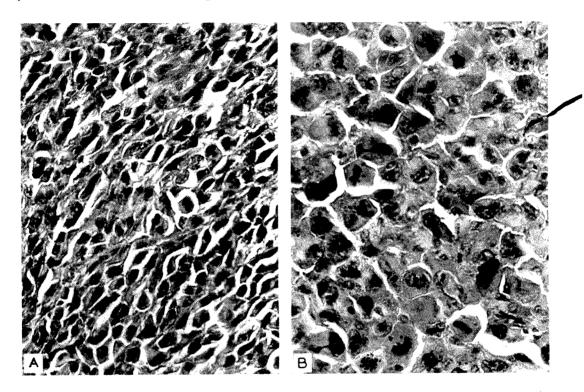


Fig. 1. Showing the relative sizes of non-irradiated and irradiated tumor cells. Photomicrographs of sectioned material were made at the same magnification.  $\mathcal{A}$  is untreated mouse sarcoma 180; B is mouse sarcoma 180 irradiated in vivo with a close of 1,500 r and allowed to remain three days in the host.

pacity of mouse sarcoma 180 was markedly destroyed (60 per cent inhibition) when the transplants were immersed in distilled water for twenty-four hours at 4–5°C. before being placed in the hosts. On the other hand, the proliferating capacity of mouse sarcoma 180 was unaffected by water when it contained salts of a Locke-Ringer solution in an isotonic amount. Furthermore, the growth capacity of mouse sarcoma 180 was inhibited 69 per cent at pH 5.0, and 61 per cent at pH 9.0. Tumor fragments immersed in solutions at pH 6.0, 7.0 and 8.0 for twenty-four hours

The transplants showed occasional spontaneous regression, such cases representing about 2 per cent of the positive growths (99 per cent). The tumor grows very rapidly (initial size of  $2 \times 2 \times 2$  mm. to a final size of about  $13 \times 18 \times 10$  mm.) and kills the animal in about three weeks.

When tumor grafts had grown for about seven days in animals and had attained a diameter of 5 to 8 mm., they were injected with sterile distilled water with a dose of 0.5, 0.75 or 1.0 cc., from two to four times daily for three to seven successive days. The injection of water was done with

a No. 24 gauge needle and by advancing the needle point in three directions within the capsule. The animals were then allowed to live as long as they would. They were fed upon Purina laboratory chows and lettuce, with as much fresh water as they would take.

The results showed that the repeated injections of sterile distilled water had no apparent influence upon the growth of transplanted tumors. The autopsies did not reveal any increase in the percentage of metastases, either local or distant, in the water injected animals over the non-reated control animals. This study included five groups of experiments involving a total of 50 tumors.

Histological examinations of a number of water treated tumor tissues show no definite changes in the structure except for larger necrotic areas than in non-treated tumor tissues (Fig. 2). The tumor cells appear to be viable. There is no noticeable cell swelling.

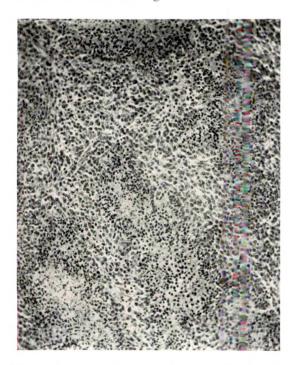


Fig. 2. A section of a water injected tumor showing no apparent alteration of the individual cells. There are, however, many scattered and irregular areas of cell degeneration.

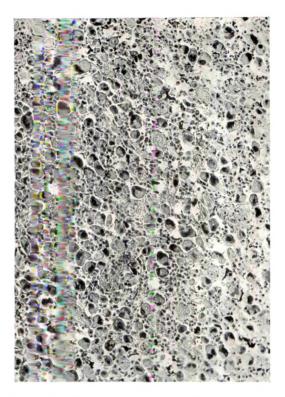


Fig. 3. I radiated mouse sarcoma 180, showing degerating tumor cells and marked lymphocytic and polymorphonuclear infiltration. No viable tumor cells can be seen in the sections.

Effect of Water upon the Growth of Irradiated Mouse Sarcoma 180. Histological examination of a number of the irradiated tumors 1,500 r) shows changes in the general structure during the first three to five days. Then the tumors undergo necrosis. Those remaining seven days in the original irradiated animals are composed of degenerating tumor cells, in which nuclei are absent or pycnotic (Fig. 3). Tumors receiving smaller doses of radiation show changes in the histologic picture but to a lesser tegree.

In the present study, we used the doses of 500, 750 and 1,000 r to determine whether appreciable changes in radiosensitivity could be produced by supplementary treatment with water. It has been shown that under normal conditions of irradiation these coses produced 3, 15 and 50 per cent tumor regressions, respectively.

When tumor grafts (mouse sarcoma 180)

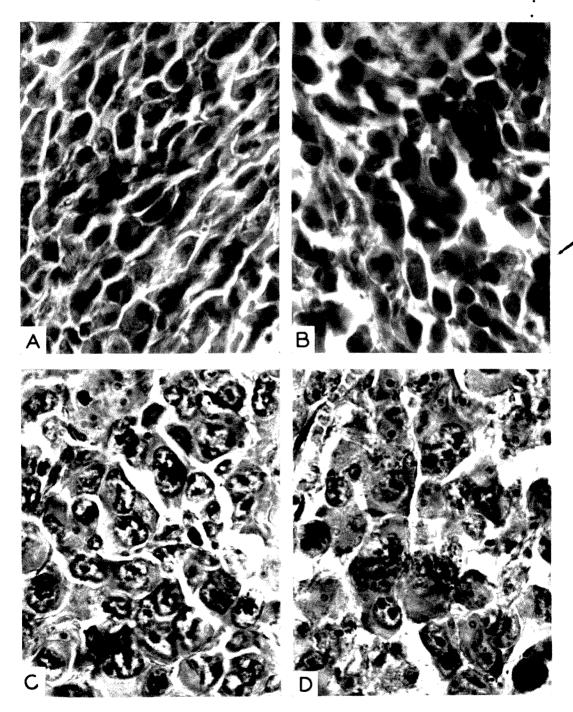


Fig. 4. Showing changes in histologic appearance in irradiated and irradiated and water treated tumors. Photomicrographs of sectioned material were made at the same magnification. A, untreated mouse sarcoma 180; B, treated with water alone; C, treated with roentgen rays alone (1,000 r); D, treated with roentgen rays (1,000 r) and water.

had grown for about seven days in animals 750, or 1,000 r in the same manner as that and had attained diameters of 5 to 8 mm., previously described.4 The conditions of they were irradiated with a dose of 500, irradiation were as follows: 200 kv.,

30 ma., 0.5 mm. copper and 1.6 mm. aluminum filter, 50 cm. distance to tumor, with an intensity of 54.4 r/min.

Then 0.5 cc. of sterile distilled water was injected into the tumor from one to four times daily for two to six successive days. The results are presented in Table 1.

 $T_{ABLE\ I}$  effect of injections of water on the growth of irradiated mouse sarcoma 180

No. of Tu- mors Used	Dose in Roent- gens	Amount of Water Used at Each In- jection (cc.)	No. of Daily Injec- tions	No. of Days In- jected	Per Cent of Tumor Regres- sion
36	500	0	0	0	3
20	750	0	0	0	15
40	1000	0	0	0	50
6	500	0.5	I	6	0
6	750	0.5	I	6	17
6	1000	0.5	I	6	33
I 2	500	0.5	2	2-3	8
12	750	0.5	2	2-3	25
12	1000	0.5	2	2-3	50
16	500	0.5	2	5-6	25
20	750	0.5	2	5-6	45
24	1000	0.5	2	5-6	75
22	500	0.5	4	4-5	36
28	750	0.5	4	4-5	61
30	1000	0.5	4	4-5	93

From the data in Table 1, it will be seen that injection of distilled water markedly increased the radiosensitivity of the tumor, especially when given as 0.5 cc. of water twice on the same day of irradiation and four times daily on three to four successive days. Thus with roentgen rays and water, 36 per cent tumor regressions with soor, 61 per cent tumor regressions with 750 r, and 93 per cent tumor regressions with 1,000 r were obtained. Roentgen rays alone in these doses produced 3, 15 and 50 per cent tumor regressions, respectively. However, injection of water once a day for several days did not change the normal course of tumor regression.

The successfully treated tumors disappeared completely in about twenty days. The time is approximately the same as that of those successfully irradiated with 1,500 r or 3,000 r but without water treatment.

Histological examinations were made on both irradiated tumors and tumors irradiated and followed by water injection (Fig. 4). In the case of 500 and 750 r, the general structure of irradiated and irraciated and water treated tumors was essentialy the same. The tumor cells were swolen but appeared to be viable. However in the case of 1,000 r, those without water treatment appeared to be normal active calls although they were markedly swolen. On the other hand, those receiving 1,000 r and water treatment appeared to be partially degenerated and not active. The swelling of tumor cells was greatest on the thire day after irradiation.

Efect of Isotonic, Hypotonic, and Hypertonic Locke-Ringer Solutions on the Growth of bracinted Mouse Sarcoma 180. The results of the foregoing experiments show that the radiosensitivity of mouse sarcoma 180 is markedly increased by injections of distilled water (a strong hypotonic medium) following local treatment with roertger rays.

In order to secure further information concerning the water and killing of tumor cells, we did the following experiments.

When tumor grafts (mouse sarcoma 180) had grown for about seven days in animals, they were irradiated with a dose of 500, 750 or 1,000 r. Then 0.5 cc. of isotonic, hypotonic, or hypertonic Locke-Ringer solution was injected into the tumors twice on the same day of irradiation and four times thereafter for four successive days.\*

The results showed that repeated injections of the isotonic or hypertonic Locke-Ringer solution, following irradiation with

<sup>\*</sup> n isomic solution contained 0.15 molecule NaCl, 0.003 molecule ICl and 0.003 molecule CaCl2 per liter. A hypotonic solution contained 0.03 molecule NaCl, 0.003 molecule KCl and 0.003 molecule CaCl2 per liter. A hypertonic solution contained 0.15 molecule NaCl, 0.003 molecule KCl and 0.003 molecule ICl2 per liter.

a dose of 500, 750, 1,000 r, did not change the normal course of tumor regression. On the other hand, the repeated injection of the hypotonic Locke-Ringer solution following irradiation definitely increased tumor regression (33, 50 and 83 per cent tumor regression, respectively). This study included three groups of experiments involving a total of 54 tumors.

### SUMMARY

- 1. The radiosensitivity of mouse sarcoma 180 was increased markedly by injections of distilled water following local treatment with roentgen rays.
- 2. Repeated injections of an isotonic or hypertonic Locke-Ringer solution into the tumors following irradiation with a dose of 500, 750 or 1,000 roentgenz did not change the normal course of tumor regression. On the other hand, injections of a hypotonic Locke-Ringer solution following local treatment with roentgen rays definitely increased tumor regression.
- 3. Daily repeated intratumor injections of sterile distilled water had no apparent influence upon the growth of tumors.

I wish to express my thanks to Dr. G. Failla for his valuable suggestions during the course of the work.

#### REFERENCES

- 1. Chambers, R., and Grand, C. G. Leucocytic infiltration of irradiated mouse sarcoma 180.

  Proc. Soc. Exper. Biol. & Med., 1937, 36, 673-675.
- 2. Failla, G. Theory of the biological action of ionizing radiations. *Cancer Probl.*, *Symposium*, 937, pp. 202-214.
- 3. FAILLA, G., and SUGIURA, K. Experimental results supporting the "fluid flow" theory of the biological action of ionizing radiations. *Science*, 1939, 89, 438.
- 4. Su-siura, K. Effect of roentgen rays on growth of rouse sarcoma 180 irradiated in vivo. *Radiology*, 1937, 28, 162-171.
- 5. Sugiura, K. Studies on radiosensitivity of mouse sarcoma 180 irradiated in vivo and in vitro. *Padiology*, 1937, 29, 352-361.
- 6. Sugura, K., and Cohen, I. Further study on cirect and indirect actions of radiation on malignant cells. 1. Transplantation of tissue cultures of mouse sarcoma 180 after exposure to roentgen rays. 11. Cultures of tumors irradiated in vivo. Radiology, 1939, 32, 71-76.
- 7. Suctura, K., and Chesley, L. C. Effect of heavy water (deuterium oxide) on viability of mouse sarcoma and melanoma. *Proc. Soc. Exper. Biol.* & Med., 1934, 31, 659-661.
- 8. SUCIURA, K. Reaction of transplantable mouse surcoma No. 180 to radiations of different wave lengths (200 kv. roentgen rays and gamma rays). Am. J. ROENTGENOL. & RAD. THERAPY, 134, 37, 614-627.



# EFFECT OF IRRADIATION ON NORMAL AND METASTATIC LYMPH NODES\*

By FRED J. TAUSSIG, M.D. St. Louis, Missouli

**D** ELATIVELY few histologic studies R have thus far been made on the effect of heavy radiation treatment upon normal and metastatic lymph nodes. Leaving out of consideration certain radiosensitive tumors, such as lymphosarcoma or transitional cell oral carcinoma, we find almost universal disappointment, regardless of the amount of radiation employed, with the results obtained in the metastatic lymph nodes of a squamous cell carcinoma. Regressions are occasionally found but they are almost always only temporary. It would seem, as Jacox has stated that the histologic study of early cancerous deposits in lymph nodes fails to reveal evidence of wholesale destruction of tumor cells and that lymphoid tissue provides a highly fertile soil for the growth of most carcinomas.

In 1904 Heineke experimented with radiation effects on the lymph nodes of pigs, rabbits and dogs and found destruction of a greater part of the lymphocytes in and around the follicles. He stated that the lympocyte is among the most vulnerable to roentgen rays. This work was later confirmed by Menetrier and Touraine. This was generally accepted as true until Quick and Cutler in 1925 came to very different conclusions. In 40 cases of oral carcinoma they studied the lymph nodes in the neck removed subsequent to heavy irradiation. Their experience was that the immediate effect of such irradiation was an increase in the mitotic figures in the germinal follicles and evidence of enlargement with hyperplasia. They conclude: "The histological picture observed in these cases is very striking. The lymphoid tissue is resistant, the lymphocytes retain their cell outline, the nuclei show light striations but retain their form. No

karydysis nor karyorrhexis is evident. The lymphoid follicles stand out prominently and appear enlarged and edematous. The germinal centers contain numerous mitotic figures; the endothelial cells appear normal." They state that Ewing had repeatedly observed that normal lymphoid tissue resists lage doses of radiation. Quick and Cutler raise the question whether this reaction is perhaps indicative of a state of heightened resistance against invasion by the tamer growth. This stimulating effect of radiation on lymphoid tissue was so muck at variance with the experience of others that some special factors may perhaps have been responsible. One of these, mentioned by Ouick and Cutler, may be the marked infection of the primary tumor in the mouth produced by the radium application. The writers do not state what interval of time elapsed between irradiation and the lymph node excision. It is possible that if this interval was a short one, the final destructive effect of heavy irraciatier upon the lymph follicles might not vet have been manifest. I could find no reports substantiating the findings of Quick and Cutler but several recent reports contradicting their findings.

Welsh in 1934 found that lymph follicles were readily destroyed by heavy irradiation. Helthusen, in an article on the biological effect of roentgen rays, writes: "The lymph follicle shows a greater radiosensitivity but at the same time also a greater capacity for regeneration, and from a few resistant cells in a relatively short time the oblicerated spaces of the reticulum of an irradiated lymph node can again become filled."

For many years I have been engaged in a systematic study of the tributary lymph nodes removed in cases of cancer of the

<sup>\*</sup> Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.

cervix and cancer of the vulva. These nodes are those of the pelvic cavity and the inguinofemoral group. It is of course possible that what applies to this part of the body is not universally true, but any marked difference in tissue reactions seems unlikely. This study is based on glands removed in 113 cases of iliac lymphadenectomy for Stage II (League of Nations' classification) cancer of the cervix, 4

obturator, external iliac, ureteral, right or left, (Fig. 1).

From an experimental viewpoint, it was a fortunate circumstance that since October, 1930, when I did my first iliac lymphadenectomy for Stage II cervical cancer there has been a progressive increase in the amount of preliminary roentgen therapy. Up to May, 1934, preliminary irradiation was practically never given. For the follow-

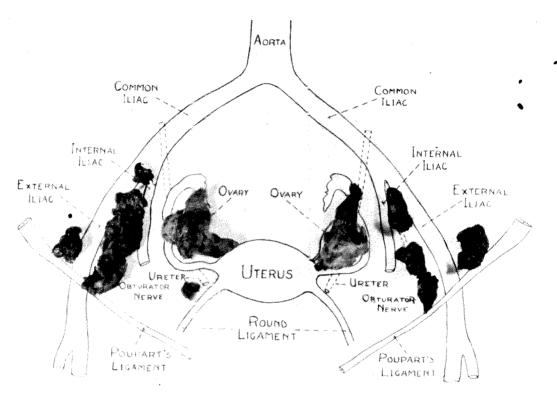


Fig. 1. Anatomic discribution of iliac lymph nodes removed surgically.

Wertheim hysterectomies with gland removal and 60 double-sided Basset lymph node operations associated with cancer of the vulva. In some of the earlier vulvar cases not all sections were saved for study, but a total of 1,039 glands were subjected to individual histologic review. Since none of the 381 vulvar glands were given preliminary irradiation, they serve only as a control. A total of 658 glands was removed in the cervix cases. Each set of glands on removal was placed in a special bottle labeled with its anatomic site (hypogastric,

ing two years, 1934–1936, the average dose was only 2,400 r. From 1936 to 1938 this was increased to a total of 5,600 r, and in the past twelve months the usual dose has averaged 7,000 r. A study of the glands with lymp 1 follicles showed a striking difference during these four periods, as seen in Table 1.

The drop from 77 per cent to 14 per cent of glands containing follicles is certainly very striking. As a rule, the interval between the conclusion of the deep roentgen treatments and the removal of the

lymph nodes was about three to four weeks. Where larger amounts of radiation were employed, there was during this interval definite regression and clearing up of the cervical carcinoma. To a slight degree the reduction of infection in the cervix may have decreased the number of germinal follicles in the glands, but could hardly have caused their complete elimination. It should also be mentioned that in recent years the total number of glands removed has been increasing, including a few that normally contain fewer follicles. Neither of these factors is of sufficient importance,

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1	r	Λ	D	т	r	1

Years	Aver- age Dose	Fol- licles Present	Fol- licles Absent	
Oct., 1930-May, 1934	none	60	18	77
May, 1934-May, 1936	2400	37	56	40
May, 1936-May, 1938	5600	75	212	26
May, 1938-May, 1939	7000	24	151	14

however, to explain the very definite decrease in germinal follicles in glands that received heavy irradiation. I know of no investigation on this subject that has heretofore used exact methods in arriving at conclusions. There is great variation in the histologic picture of lymph glands in different individuals and even in the same individual. Unless each gland is separately reviewed and the percentage of these containing follicles calculated on a large scale, deductions cannot fairly be drawn. A point of further interest was that when we compared the germinal follicles in non-irradiated glands with follicles that had been irradiated, marked differences were noted in many cases (Figs. 2 and 3). In the nonirradiated glands, the follicles had a definite circular or ovoid outline with a rim of several rows of small, deeply staining lymphocytes surrounding the epithelioid cells in the center of the follicle. In the irradiated glands this lymphocytic capsule

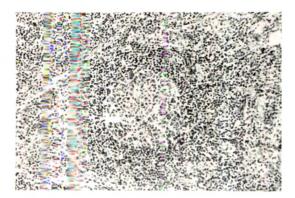
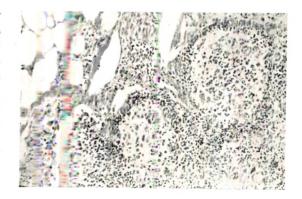


Fig. 2. Non-irradiated lymph node with normal germinal follicles.

of the follicle was often broken and the germinal cells showed definite evidence of part al liquefaction. This disintegration of the follicles can probably be considered as due to an irradiation effect. All in all, therefore, we can fairly conclude that irradiation produces a destruction of the germinal follicles in pelvic lymph glands in direct proportion to its intensity.

The question naturally arises as to the permanency of this destructive effect. Holhusen says that there is an inherent capacity for regeneration of follicles in such irradiated glands. Some confirmation of this statement was to be found in our lymph mode studies. Taking only the 47 cases since May, 1936, those in which a destructive dose over 5,600 r had been given, I found that in 7 cases the lymph node removal had for special reasons not



I.G. 3. Irradiated lymph node with disintegrated follicles.

been done until from three to six months after the irradiation. This should allow sufficient time for regeneration. It was found that although the percentage of follicle-containing lymph nodes in the entire 47 cases during this period was 21 per cent, the 7 cases in which operation was delayed had an incidence of follicle-containing lymph nodes of 41 per cent (14 out of 34 glands). These figures are of course too small to be conclusive, but support the theory of Holthusen regarding such regeneration of the germinal follicles.

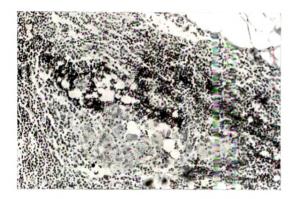


Fig. 4. Minute subcapsular metastasis in a hypogastric lymph node that grossly seemed quite normal.

It would seem, therefore, that deep roentgen therapy applied to the pelvic region produces a definite effect on the normal germinal follicles. Turning now to a consideration of the metastases in these glands, we find that the effect of irradiation is, relatively speaking, insignificant.

Dividing the II3 cases chronologically into the periods of little or no irradiation before operation from October, 1930, to May, 1936, and that of heavy preoperative irradiation (5,600 to 7,000) from May, 1936, to May, 1939, we find that in the 47 cases of the first period cancer metastases were present in the lymph nodes I4 times, equivalent to exactly 30 per cent. During the second period when heavy preoperative irradiation was employed, we found metastases in 22 out of 66 cases, equivalent to 33.3 per cent; slightly more often, therefore, than in the non-irradiated cases. In

the total series of 113 cases, 36 showed metastases, an average of 31.9 per cent.

These figures would indicate an accidental variation in the number of cases that showed metastatic lymph nodes but certainly no diminution in their number as a result of preceding roentgen treatment. The histologic study of lymph nodes subjected to heavy irradiation tended to confirm the absence of any appreciable effect on the cancer metastasis. While the cancer cells in the cervix showed marked liquefaction necrosis and vacuolization, the cancer in the lymph node only in rare instances showed even the slightest evidence of destructive changes. The metastases, as a rule, consisted of nests of fairly well differentiated squamous cell carcinoma, often appearing less malignant than the primary tumor in the cervix. Many of these metastases were microscopic in size. Certainly the size and hardness of the lymph glands were not a definite index of the presence of metastasis. Many hard fibrous or hyalinized lymph glands were found free of disease and occasional small soft glands were found to contain nests of cancer cells. Recently I removed a soft hypogastric lymph node only 2-3 mm. in diameter that contained a well developed cancer metastasis (Fig. 4). The more I operate on these cases the more convinced I am that the fact that cancer was not found in a lymph node does not mean that cancer was not present. Only by the tedious process of serial sections of all lymph nodes removed could such a statement be justified. It is false to assume that, because in a little over two-thirds of the cases in which lymph nodes were removed no cancer was found, the operative removal was unjustified. In breast cancer we certainly have ample evidence of the value of routine lymph node removal, regardless of the presence of metastasis. The same has, I think, now been established in the case of cervical cancer. Heretofore the high operative mortality has been held against such surgical removal of lymph nodes. The reason of this high mortality lay, however, not in the

gland removal, but in the associated radical hysterectomy. One thing that I have now proved by my operation of iliac gland removal without hysterectomy in Stage II cancer of the cervix is that it is not a dangerous procedure. In 113 operations of this kind done in the past eight and a half years, only 2 patients have died, a mortality of only 1.77 per cent. Not only has this operative removal of the tributary lymph nodes in border line cervical cancer associated with irradiation of the primary lesion been shown to be safe, but as a larger number of five year cases are now being gathered for report, the ultimate results have been shown to be beneficial. I now have 19 cases operated on over five years ago and 10 of these have survived this period without evidence of a recurrence, a survival rate of 52.5 per cent. Three out of the eight cases that showed cancer metastasis in the glands survived the five year period. During this same time, and in the same institution (Barnard Free Skin and Cancer Hospital), 35 cases of Stage II cancer of the cervix were treated by irradiation alone with a survival rate of only 20 per cent. In both groups the radiation dosage and methods were identical, yet when the lymph nodes were removed in addition to the irradiation, more than twice as many survived the five year period. It is interesting also to compare my results with the report of Frazell from Healy's clinic. In the the group of border line cases treated over five years Frazell found only 6 living out of 19, a cure of 31.5 per cent. Voltz, in 310 cases of Stage II cancer of the cervix treated

by irradiation alone, had a five year survival of 22.3 per cent.

I am willing to grant that the exact number of cures by this iliac gland removal may fluctuate somewhat in later reports. It may fall as low as 40 per cent, but certainly thus far we can fairly conclude that until newer methods of eradicating metastases in lymph nodes by irradiation are found, surgical ablation of these glands most commonly involved is not only justified, but definitely to be recommended.\*

### REFERENCES

- 1. Ewing, J. Quoted by Quick and Cutler, ref. 6.
- 2. Frazzle, E. L. Correlation of calculated tumor doses and five-year survivals in radiation therapy of cancer of the cervix. Am. J. Roent-Genol. & Rad. Therapy, 1938, 39, 861-865.
- 3. HEINEKE, H. Experimentelle Untersuchungen über die Einwirkung der Röntgenstrahlen auf innere Organe. Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1904, 14, 21.
- 4. HOLTHUSEN, H. Die allgemein-biologische Wirkung der Röntgenstrahlen. Strahlentherapie, 1938 52, 228-239.
- 5. Jacox, H. W. Irradiation of cervical glands in carcinoma of mouth and lip. Am. J. Roent-GENGE. & RAD. THERAPY, 1938, 39, 778-782.
- 6. QUICK, D., and CUTLER, M. Radiation reaction of metastatic squamous cell carcinoma in cervical lymph nodes. Am. J. Roentgenol. & Rad. Therapy, 1925, 14, 529-540.
- 7. TAUSSED, F. J. Study of lymph glands in cancer of the cervix and cancer of the vulva. Am. J. Oest & Gynec., 1938, 36, 819-832.
- 8. Tausse, F. J. Lymph gland removal in cancer of the cervix. J. Michigan M. Soc., 1938, 37, 1074-1078.
- Welsh A. M. Cell reactions in lymph nodes draining sites of primary carcinoma. M. J. Australia, 1934, 2, 345-347.
  - \* For discussion see page 571.



## RADIUM TREATMENT OF CARCINOMA OF THE CERVICAL STUMP\*

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SINCE Chrobak, in 1896, first called attention to cancer developing in the cervical stump after subtotal hysterectomy as a definite clinical entity, a considerable amount of literature has evolved on this important subject. A great many excellent articles have been devoted to the incidence, prevention and treatment of this serious condition. C. H. and C. W. Mayo, Masson, 3 Spencer,4 von Graff5 and Polak6 are among the authorities who have held the belief that cancer occurs in the retained cervix often enough to justify panhysterectomy instead of the more commonly employed subtotal hysterectomy for uterine myomas or other conditions that require removal of the uterus. In addition, Mayo and Dixon<sup>7</sup> have pointed out that, like the prostate gland, the cervix may become a focus of infection; the probability that cancer will develop or that infection will spread from the retained cervix is an argument for panhysterectomy. Masson and Spencer, among others, have stated that the risk of panhysterectomy in skilled hands is little more than that of the conservative operation, especially considering the potentialities of the retained cervix for the development of malignant lesions.

On the other hand, other authorities have considered the incidence of cancer of the retained cervix too small to overbalance the greater surgical risk of panhysterectomy. Baer, Scheffey, Healy and Arneson, Stein, and Leonard are among those who have not favored abandoning the conservative operation for panhysterectomy with the higher mortality rate associated with the latter and the loss of support to the pelvic floor, and so forth. Estimations of the incidence of carcinoma of the cervical stump vary tremendously;

for instance, from 0.03 per cent quoted by Scheffey9 from the German literature after the study of several thousands of supravaginal hysterectomies, to 4.1 per cent quoted by von Graff<sup>5</sup> from radiologic literature. This discrepancy is to be expected, Lowever, because surgeons must trace each operative case, often for more than a quarter of a century, whereas at radium centers in studies of carcinoma of the cervix a much larger series is seen and the lesion often occurs many years after the conservative operation has been performed. Many surgeons such as C. H. and C. W. Mayo<sup>2</sup> and Howard A. Kelly<sup>12</sup> have held the belief that when a supravaginal hysterectomy is performed, a thorough cupping or coning out of the cervical mucosa lessens the possibility of the subsequent development of malignant changes. Polak6 has disputec this; he has contended that nearly all carcinomas of the cervical stump are squamous cell epitheliomas springing from the muccus membrane of the vaginal portion of the cervix, and that to cone out the cervical canal is not sufficient protection.

We are not qualified to take sides in this argument regarding pelvic operations, but we are interested in the clinical aspects of carcinoma of the cervical stump shown by patients who present themselves for treatment; we are also interested in the treatment that we have been employing in the past, and in the results so far achieved.

At the Fifth International Congress of Radiclogy in 1937, we<sup>13</sup> presented a survey of treatment and results in 1,491 cases of carcinoma of the cervix in which treatment with radium and roentgen rays was given in this department of the Mayo Clinic from January 1, 1915 to December 31, 1929.

For this present study we have analyzed

<sup>\*</sup> Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.

in respect to treatment and results the cases of carcinoma of the cervical stump contained in that group with the addition of 7 cases in which treatment was given in 1930.

Adding the cases encountered in 1930, there were 1,676 patients, who had carcinoma of the cervix, referred for radium treatment. A preliminary survey revealed that in the total of 1,676 cases there were 108 cases of carcinoma of the cervical stump. However, by rejecting those patients not treated at the Mayo Clinic or patients who had only a biopsy and palliative cauterization performed, in the early days of radiologic practice, a total of 90 patients with this diagnosis is left.

Another differential problem was encountered. As Schulze,<sup>14</sup> Branscomb,<sup>15</sup> Spencer, and others have pointed out, carcinomas may be overlooked at the time of the initial operation. Spencer, with Noble and Schlottländer,4 examined 900 myomatous uteri removed by the method of panhysterectomy, and found, in 2 per cent of the specimens, carcinoma of the cervix which had been previously overlooked. In addition there is the possibility of a metastatic carcinomatous lesion or a recurrent lesion in the cervical stump from the primary site of an excised cancer of the fundus uteri or ovary. These possibilities present a complicated therapeutic problem and prognosis, just as the treatment and prognosis of a primary lesion of carcinoma of the breast, for instance, differs from treatment and prognosis of a distant metastatic lesion from carcinoma of the breast. Hence, to eliminate as far as possible overlooked epitheliomas of the cervix and metastatic lesions from fundal and ovarian cancer, we adopted Sharples'16 dictum, that if carcinoma is not diagnosed in the retained cervix until two years after the subtotal hysterectomy, it is probably a genuine instance of malignancy of the cervical stump. This view was also advanced by Nuttall and Todd,17 who termed carcinomas discovered less than two years after subtotal hysterectomy as "coincident

TABLE I INCIDENCE

Patients with carcinoma of the cervix, treated with radium (1915 to 1930, in- clusive)	1676
Of this group, diagnosis of carcinoma of	
the cervical stump made in	(6.4%)
Patients treated with radium	99 (5.9%)
Probably genuine stump cases (diagnosed two years or more after opera-	
tions)	(3.4%)

cases," or dual carcinomas and if discovered more than two years afterward, as probably genuine cases of stump carcinoma.

After satisfying this dictum in our present study, 57 probably genuine cases of carcinoma of the cervical stump remain, representing 3.4 per cent of our entire series of 1,676 carcinomas of the cervix (Table 1).

The interval between the subtotal hysterectomy and the diagnosis of cancer of the retained cervix varied from two to twenty-nine years in this group of 57 cases; more than twenty years in 5 instances, and between ten and twenty years in 15 additional cases. Only 9 of the 57, or 15.8 per cent, had had the antecedent operation at The Mayo Clinic. The youngest of the 57 patients was thirty-four years of age, the oldest, sixty-four years, and the average age was 51.2 years.

A study of the fertility of the 57 patients yielded the results shown in Table 11. The incidence of nonfertility (21.4 per cent) agrees with that reported by Branscomb<sup>15</sup> (20 per cent) and Meigs<sup>18</sup> (23 per cent) in studies of large series; 46 and 26 cases, respectively.

The antecedent operation, in more than half of the cases, was a subtotal hysterectomy for uterine myomas or for menorrhagia. An analysis of our own cases in relation to the incidence of the various causes of

Table II

INCIDENCE OF FERTILITY IN CASES OF CARCINOMA
OF THE CERVICAL STUMP

n '	Patients		
Pregnancies	Number	Per cent	
0	12	21.4	
ì	9	16.1	
2	8	14.3	
3	8	14.3	
4	9	16.1	
5	2	3.6	
6	5	8.9	
7	ī	1.7	
8	2	3.6	
Total	56	100	
No data	ľ		

antecedent operations is found in Table III. Thus, in all, 33 of the 57 patients had subtotal hysterectomy for uterine myomas or for menorrhagia, and 5 additional patients had that operation for pelvic inflammatory resions. In 9 cases, malignancy may have been present.

The stage of the lesion, depicting anatomically the extent of involvement, is important in treatment and prognosis. Our 57 cases are classified according to our

TABLE III

INCIDENCE OF VARIOUS CAUSES OF ANTECEDENT
OPERATIONS IN CASES OF CARCINOMA OF
THE CERVICAL STUMP

	Cases in which ante- cedent operations were performed			
Reason for operation	1 IVIAVO		Total cases	
Uterine myomas	23	6	29	
Menorrhagia	4	0	4	
Inflammatory conditions	3	2	5	
Suspected malignancy	8	1	9	
Unknown	10	0	10	
Total	48	9*	57	

<sup>\*</sup> Cases in which an antecedent operation was performed at the Mayo Clinic represented 15.8 per cent of the total number.

TABLE IV

CARCINOMA OF THE CERVICAL STUMP; STAGE OF
LESION BEFORE TREATMENT

Stage	Cases	Per cent
1	0	0.0
11	11	19.3
111	30	52.6
IV	16	28.1
Total		100

previously published criteria for the treatment of cancer of the cervix. Briefly, in Stage 1, cancer is limited to the cervix; in Stage 11, there is extension beyond the cervix to the vaginal walls or into one or both parametria, without fixation; in Stage 111, definite fixation exists through one or both parametria and in Stage 112 the primary lesion is usually fixed and distant metastatic lesions often are present. The results of analysis of our series according to the findings at the time of the initial examination are given in Table 112.

Thus, we had a manifestly difficult group, with 80 per cent of the lesions representing advanced stages. Results of biopsies before treatment in the 57 cases are given in Table v. In the early years covered by this study, biopsies were not routinely performed. Hence, in 13 of these cases (22.8 per cent), biopsy was not per-

 $T_{ABLE}\ V$  carcinoma of the cervical stump; findings on biopsy before treatment

No biopsy (22.8%, early years)	13
Colloid carcinoma	1
Squamous cell epithelioma, not graded	] 3
Adenocarcinoma, not graded	] 3
Squamous cell epithelioma, Grade 2	$\epsilon$
Squamous cell epithelioma, Grade 3	16
Squamous cell epithelioma, Grade 4	10
Adenocarcinoma, Grade 1	2
Adenocarcinoma, Grade 2	I
Adenocarcinoma, Grade 4	1
Squamous cell epithelioma and adeno-	
carcinoma, Grade 3	1
Total	57

formed; however, all were clinically malignant lesions, and 11 of the 13 patients died of cancer. It is interesting to note that of the 44 biopsies, 36 (82 per cent) revealed squamous cell epitheliomas; also, of the 37 graded specimens, 28 (75 per cent) were Grades 3 and 4, comparing favorably with the percentages calculated for the group of 1,676 cases.

Treatment of carcinoma of the cervical stump is a difficult problem. All of these lesions come under our "modified" group in classification of treatment of carcinoma of the cervix, as previous operation has ablated the fundus of the uterus and has imposed a limited form of treatment. Results of radium therapy in stump cases vary greatly in the reports from different clinics. Von Graff, in 1934, reviewed all of the literature and has found the rate of cure by irradiation or by operation and irradiation in 428 cases to be 9.3 per cent. Meigs<sup>18</sup> described treatment in 10 cases, with a rate of cure of 7.6 per cent for four years. Nuttall and Todd reported a series of 20 cases in which a five year cure was obtained in 50 per cent. In 31 cases in which treatment was given in George Gray Ward's service, Sackett<sup>19</sup> quoted results over a period of five years of survival in 48.4 per cent of cases. Healy and Arneson, 10 in treating 36 patients, obtained a five year cure in 14 per cent.

Dangers of treatment have been cited by many radiologists. Nuttall and Todd<sup>17</sup> have emphasized that, in their treatment, radium is never placed in the cervical canal, but is packed off from the rectum and bladder. Jeanneney<sup>20</sup> stated that care is necessary in applying radium because of the proximity of intestinal loops; Phaneuf<sup>21</sup> has warned of increased danger of vesicovaginal and rectovaginal fistulas after treatment because by ablation of the fundus uteri a heavy source of filtration is removed. Counseller and Foor<sup>22</sup> reported the closure of an enterovaginal fistula which developed in a cervical stump a year after radium treatment; he warned that a loop of bowel may be too closely adherent

Table VI

CARCINOMA OF THE CERVICAL STUMP; DURATION

OF LIFE AFTER LAST RADIATION TREATMENT

Duration of life	Patients	Per cent
Less than 1 year	13	22.8
Less than 2 years	14	24.6
From 2 to 5 years	15	26.3
From 5 to 10 years	9	$26.3$ $\begin{cases} 15.8 \\ 10.5 \end{cases}$
More than 10 years*	6	20.3 10.5
Total	57	100.0

<sup>\*</sup> Includes patients now living 19, 17, 16 and 12 years after treatment.

to the stump of the cervix.

Treatment in our 57 cases carried out over a period of fifteen years, has shown alterations in our technique from time to time. Treatment was mainly with radium, followed with roentgen therapy. The majority of patients received one course of radium therapy, followed by two courses of roentgen therapy, about three months apart. One course of radium therapy, followed by roentgen therapy, was given in 24 cases, two courses a few months apart in 10 cases, three courses in 5 cases, and more than three courses in 8 cases. Seven patients had radium treatment only, and 3 had roentgen therapy only. Prior to 1920, radium treatment consisted of the introduction of highly filtered tubes of radium into the vagina and rectum. Since 1920, the treatment has consisted of three or four applications in the cervical canal and two or three vaginal treatments, totalling approximately 4,000 millicuriehours over a period of about two weeks. Roentgen therapy consisted, up to 1923, of moderate voltage treatments, approximately 135 kv.; from 1923 to the present, high voltage has been used, approximately 200 kv., over four to six portals, with 0.75 mm. copper and I mm. aluminum filtration, at a distance of 50 cm., 560 r to the field. The results of treatment in the 57 cases are recorded in Table VI.

Hence, patients who live beyond the five year period, usually judged to be "cures," numbered 15, or 26.3 per cent of

TABLE VII CARCINOMA OF THE CERVICAL STUMP; ANALYSIS OF THE 15 "CURED" CASES

Grade of lesion	Cases
No biopsy	2
Squamous cell epithelioma, Grade 4	3
Squamous cell epithelioma, Grade 3	6
Squamous cell epithelioma, Grade 2	1
Adenocarcinoma, Grade 2	I
Adenocarcinoma, Grade I	I
Adenocarcinoma (ungraded)	1

the total number. Of the 15, five had died subsequently; one of a heart attack nine years after the last treatment, without evidence of recurrence of the malignancy, and one of pneumonia, eleven years after treatment, also without evidence of cancer. In the other 3 cases, data regarding the cause of death were not available. The results of analysis of these 15 so-called cured patients in regard to biopsy are given in Table vii. This distribution agrees closely with that of the total group of 57 cases. Of the 13 microscopic studies, 77 per cent revealed squamous cell epithelioma; of the graded lesions, 75 per cent were grades 3 and 4.

The distribution of the 15 "cured" cases, according to the stage of the disease, differed considerably from that of the total group. Eighty per cent of the 57 cases represented Stages III and IV, whereas, of our 15 "cured" cases only 60 per cent represented Stages III and IV (Table VIII).

TABLE VIII CARCINOMA OF THE CERVICAL STUMP; DISTRIBUTION ACCORDING TO STAGES

Stage	Cases	Per cent
I II III	6 6 3	0 40 40 20
Total	15*	100

<sup>\*</sup> Five year cures according to stage before treatment:

54.55% of Stage II. 20.00% of Stage III.

We do not have time for description of individual cases, but one case is unusually interesting and merits mention. A patient, aged sixty-one, had had a hysterectomy for uterine myomas two years previously; we treated the patient in 1930 with radium and roentgen rays for squamous cell. epithelioma of the cervical stump, Stage III, Grade 3. This lesion cleared up completely; but the patient returned in 1932; she then had adenocarcinoma of the rectum, Grade 2. This was treated with radium, and she has remained well and free of recurrence.

Let us now consider briefly the "coincident cases," the 42 cases in which the

TABLE IX CARCINOMA OF THE CERVICAL STUMP; "COINCIDENT" CASES DIAGNOSED LESS THAN TWO YEARS AFTER OPERATION

Stage	Cases	Per cent
I	0	0.0
II	3	7.1
ш	21	50.0
17	18.	50.0 42.9
Total	42	100.0

diagnosis of cancer was made a month to two years after removal of the uterus; with this brief interval we may assume carcinoma to have been present when the hysterectomy was performed. The patients in this group were younger than those in the group of cases in which true carcinoma of the stump was found; the average age in the former group was 43.8 years. In 17 cases, or 40 per cent, in which treatment was given in the early years, biopsy was not performed. Of the remainder, 87.5 per cent were cases of squamous cell epithelioma, and 79 per cent of the lesions were Grades 3 or 4. The stage of the disease was farther advanced than in the true stump cases; 93 per cent were in Stages III or IV (Table 1x).

The results of treatment were as listed in Table x. The results of treatment in these cases have not been so good as in the

<sup>18.75%</sup> of Stage IV.

true stump cases. Instead of 26.3 per cent of cures as in the true stump cases, we obtained 21.4 per cent of cures in this group; but whereas in the true stump cases 22.8 per cent of the patients died within the first year after treatment, in the "coincident" class, 54.8 per cent died within the first year. As Nuttall and Todd<sup>17</sup> pointed out, we expect a poor result in the "coincident cases," a result comparable to incomplete surgical excision of a carcinomatous lesion anywhere in the body.

One patient in this "coincident group" is of special interest. In 1929, she had had a "chemical hysterectomy" at The Mayo Clinic for menorrhagia (the only case of this type of operation included). One and a half years later she returned, and was found to have advanced carcinoma of the cervix, squamous cell epithelioma, Grade 4. This was treated with one course of radium and two courses of high voltage roentgen therapy in the autumn of 1930. The carcinoma disappeared and she remained well and free of symptoms until the autumn of 1937, seven years later, when an extensive recurrence (or a new malignant lesion) appeared in the cervix. A limited palliative radium treatment was given but she died of carcinoma in August, 1938.

Another important feature in this study should be an attempt to gauge whether better results have attended our changes of technique throughout the years (Table XI). Of the 57 cases of carcinoma of the cervical stump, in 14 treatment was given

TABLE X

CARCINOMA OF THE CERVICAL STUMP; "COINCIDENT"

CASES, LENGTH OF LIFE AFTER TREATMENT

Duration of life	Patients	Per cent
Less than 1 year	23	54.8
Less than 2 years	6	14.3
From 2 to 5 years	4	9.5
From 5 to 10 years	5	(11.0
More than 10 years*	4	21.4 9.5
Total	42	100.0

<sup>\*</sup> Includes patients living 14 and 13 years after treatment.

Table XI

CARCINOMA OF THE CERVICAL STUMP

(57 cases)

Period	No. treated	Cured	Died in 1st year	
1915–1919	14	4	2	
1920-1924	17	3	4	
1925-1930	26	8	7	
"Coin	cident" cases	s (42 cases	)	
1915-1919	IO	0	10	
1920-1924	12	2	4	
1925-1930	20			

in the first five years, 1915 to 1919 inclusive. Of these, 2 died within the first year. and there were 4 "cures"; that is, the patients remained in good health for more than five years. From 1920 to 1924, inclusive, 17 patients received treatment; 4 died in the first year and 3 were cured. From 1925 to 1930, inclusive, of 26 patients treated, 7 died in the first year, but 8 were cured. Thus, of 15 cured patients, only 4 were treated between 1915 and 1919, inclusive, and more than half were treated in the span from 1925 to 1930. The 42 "coincident" cases show a greater difference. In the years 1915 to 1919, inclusive, 10 patients were treated and all died within the first year. From 1920 to 1924, inclusive, 12 received treatment and 4 died within the first year, but 2 patients were curde. In the final group, from 1925 to 1930, inclusive, of 20 patients treated, 9 died in the first year, but 7 cures were obtained. Thus, of the 9 cures, not one was obtained in the first five year span, 2 were obtained in the second, and 7 in the third.

## CONCLUSIONS

Carcinoma of the retained cervix, subsequent to a supravaginal hysterectomy, is a very serious condition. When discovered, most of the lesions are in advanced stages, and the prognosis is poor. This condition occurs at the time of the menopause, or slightly later, and occurs most often after a subtotal hysterectomy for uterine fibromyomas. Undoubtedly, as Branscomb<sup>15</sup> has suggested, when uterine myomas are known to be present in cases of vaginal bleeding, investigation of possible causes of vaginal bleeding other than uterine myomas may not be considered, and a coincidental cancer of the cervix may be easily overlooked.

For the surgeon who must decide between performing a subtotal hysterectomy and a panhysterectomy when removal of the uterus is necessary, acquaintance with the true incidence of cancer in the cervical stump is of vital importance. Unfortunately, this information is difficult to obtain. The follow-up of cases by surgical clinics yields a very low incidence, which is natural when we remember that patients may have to be traced for two or three decades. Radiologic clinics, in the treatment of carcinoma of the cervix, have found a far higher incidence of malignancy in the retained stump than have surgical clinics.

In our experience, among 1,676 patients who had carcinoma of the cervix treated with radium at the Mayo Clinic from 1015 to 1930 inclusive, 108 were diagnosed as carcinoma of the cervical stump. By eliminating a few patients who were not treated here, or who received treatment by cauterization only, 99 cases remain, 6.4 per cent. However, further pruning was necessary. We agree with Nuttall and Todd, 17 and with Sharples,16 that if two years or longer have elapsed between subtotal hysterectomy and the discovery of the malignant lesion in the retained cervix, the lesion is probably a true carcinoma of the cervical stump, and not a "coincident" or dual carcinoma which was present before the operation was performed.

On this basis, we had 57 cases remaining, or 3.4 per cent of the total series. The interval between operation and the diagnosis of malignancy was more than twenty years in 5 cases, and between ten and twenty years in 15 additional cases.

We found, on analysis, that careful radium and roentgen therapy does yield

worth-while results, which have been improving with changes in technique. Cure for more than five years was obtained in 26.3 per cent of the cases. These patients are now living and well nineteen, seventeen, sixteen and twelve years, respectively, after their last treatment, although the extent of the lesion on diagnosis had represented an advanced stage (80 per cent were in Stages III or IV) and the grade of the cancer was high in cases in which biopsies had been taken (75 per cent were Grades 3 or 4). Incidentally, patients who have never been pregnant are not immune to cancer of the cervix. In 21 per cent of cases in our series a history of nonfertility was obtained.

Results were not so fortunate in the "coincident" cases, or dual malignant lesions, those discovered less than two years after operation with carcinoma probably coexisting at the time of the operation. As Nuttall and Todd17 had emphasized, results in these are comparable to the results of incomplete operation for a malignant lesion anywhere in the body. Although the five year survivals in our series were only 5 per cent less (21.4 per cent), more than half of the members of the group died within the first year after treatment (54.8 per cent), contrasted with 22.8 per cent of the true carcinomas of the stump. The lesions were more advanced when first seen; only 7 per cent were in Stage II, contrasting with the true stump group in which 20 per cent were in Stage II.

Hence, although in the presence of carcinoma of the cervical stump careful irradiation can accomplish much and the prognosis is not utterly bad, much remains to be accomplished in the way of prevention. The seriousness of carcinoma of the cervical stump must be publicized and reemphasized. Whenever a subtotal hysterectomy is performed, a conscientious examination of the cervix should be a requisite. After such an operation, the patient should have pelvic examinations at stated intervals, and should be instructed

to come voluntarily for attention at any time, if vaginal bleeding occurs.\*

### REFERENCES

- 1. CHROBAK, R. Beitrag zur Kenntniss und Therapie der Uterusmyome. Monatschr. f. Geburtsh. u. Gynäk., 1896, 3, 177-185.
- 2. Mayo, C. H., and Mayo, C., Jr. Carcinoma of the cervical stump following subtotal hysterectomy. *Ann. Surg.*, 1931, 93, 1215-1219.
- 3. Masson, J. C. Total versus subtotal abdominal hysterectomy. Am. J. Obst. & Gynec., 1927, 14, 486-492.
- 4. Spencer, H. R. Remarks on total abdominal hysterectomy for myoma of the uterus; with special reference to cancer of the cervix after the subtotal operation. *Brit. M. J.*, 1932, *I*, 1157–1160.
- 5. von Graff, Erwin. Cancer of the cervical stump following subtotal hysterectomy. Am. J. Obst. & Gynec., 1934, 28, 18-32.
- POLAK, J. O. Incidence of cancer in the cervix occurring in the retained stump after supracervical amputation for fibroids. New York State 7. Med., 1921, 21, 45-47.
- State J. Med., 1921, 21, 45-47.
  7. MAYO, C. H., and DIXON, C. F. The cervix as a focus in chronic disease. Minnesota Med., 1927, 10, 671-673.
- 8. BAER, J. L. The cervix uteri in obstetrics and gynecology. J. Am. M. Ass., 1938, 111, 2357-2360.
- Scheffer, L. C. Carcinoma of the cervical stump. 7. Am. M. Ass., 1936, 107, 837-843.
- stump. J. Am. M. Ass., 1936, 107, 837-843.

  10. HEALY, W. P., and Arneson, A. N. A study of carcinoma of the cervical stump developing after subtotal hysterectomy. Am. J. Obst. & Gynec., 1935, 29, 370-383.
- II. Stein, Arthur. Cervical stump carcinoma following supravaginal hysterectomy; report of

- two cases with a discussion of the advisability of subtotal hysterectomy. Am. J. Surg., 1928, 5, 340-344.
- LEONARD, V. N. On the development of malignant disease of the cervical stump after supravaginal hysterectomy. Ann. Surg., 1913, 58, 373-383.
- 13. Bowing, H. H., and FRICKE, R. E. Carcinoma of the uterine cervix; survey of treatment and results in 1,491 cases. Am. J. ROENTGENOL. & RAD. THERAPY, 1938, 40, 47-51.
- 14. Schulze, Margaret. Postmenopausal hemorrhage. California & West. Med., 1933, 39, 158-161.
- 15. Branscomb, Louise. The occurrence of cancer in the uterine cervical stump after supravaginal hysterectomy. Am. J. Obst. & Gynec., 1930, 20, 66-69.
- 16. Sharples, C. W. Carcinoma of cervical stump following partial hysterectomy. Northwest
- Med., 1927, 26, 77-78.

  17. NUTTALL, J. R., and TODD, T. F. The prognosis in carcinoma of the cervical stump after subtotal hysterectomy; a critical analysis of 38 cases. J. Obst. & Gynaec. Brit. Emp., 1935, 42, 860-866.
- 18. Meigs, J. V. Carcinoma of the retained cervix or subtotal vs. total hysterectomy. Am. J. Obst. 83 Gynec., 1036, 31, 358-366.
- Obst. & Gynec., 1936, 31, 358-366.

  19. Sackett, N. B. The prognosis of cancer of the cervix treated by irradiation. New York State J. Med., 1935, 35, 1153-1158.
- 20. JEANNENEY, G. Le cancer du col restant après hystérectomie sub-totale. Rev. franç. de gynéc. et d'obst., 1929, 24, 273-282.
- 21. Phaneuf, L. E. Carcinoma of the cervical stump. Am. J. Surg., 1935, 29, 479-480. 22. Counseller, V. S., and Foor, C. G. Entero-
- 22. Counseller, V. S., and Foor, C. G. Enterovaginal fistula following application of radium to the cervical stump; malaria following pelviolithotomy. S. Clin. North America, 1934, 14, 705-708.



<sup>\*</sup> For discussion see page 571.

# IRRADIATION OF CARCINOMA OF THE CERVIX UTERI IN PREGNANCY\*

By ABRAHAM STRAUSS, M.D. CLEVELAND, OHIO

SINCE 1909 when Williams published the results of his experiences together with a summary of the literature on the treatment of carcinoma of the cervix uteri during pregnancy, irradiation has become a factor. This review is intended to investigate what progress, if any, modern sur-

of view—surgery and obstetrics. The latter has two considerations—the mother and the child.

It is a well known fact that cancer of the cervix most commonly occurs after the age of fifty when pregnancy is exceedingly rare. Therefore, in dealing with cases of preg-

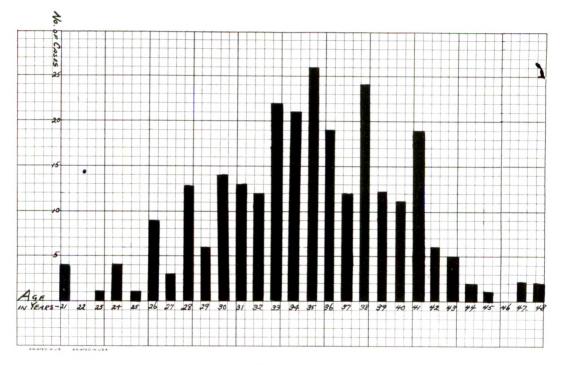


CHART I

gery has made and what radium and roentgen radiation have added to the treatment.

Most authorities agree today that carcinoma of the cervix is treated as well if not better by irradiation than by surgery in most instances. The question whether the concomitant pregnancy changes this dictum remains to be answered by the results of experience. It is obvious that this lesion has to be considered from two points

nancy complicated with cancer we usually deal with a younger group of patients. The oldest person in this series was forty-eight and the youngest was twenty-one, at which age there were four. Of 264 cases where the age was mentioned 175, or 66 per cent, were in the fourth decade (Chart 1).

The incidence of cervical carcinoma among pregnant women varies from the figures of Mussey 1 in 437, to 1 in 12,383 given by Hirst. It is quite evident that

<sup>\*</sup> Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.

very few doctors not connected with a large obstetrical clinic see the two conditions in association, yet it is important to watch for that one case so that it may be properly treated.

This report is based on 280 cases published between 1895 and 1936 inclusive, adding one unpublished case treated by Pomeroy, and two by the author one of which is mentioned in the monograph by Bubis.

1

test, or diagnosed by biopsy and which is discovered in the latter half of pregnancy may be said to have originated after conception. On the other hand, a growth involving the whole cervix or inoperable in the first half of pregnancy undoubtedly preceded conception.

But to judge the age of the cancer by its extent calls forth the age old discussion of the effect of pregnancy on the rate of the growth of the cancer. Zweifel's classic clini-

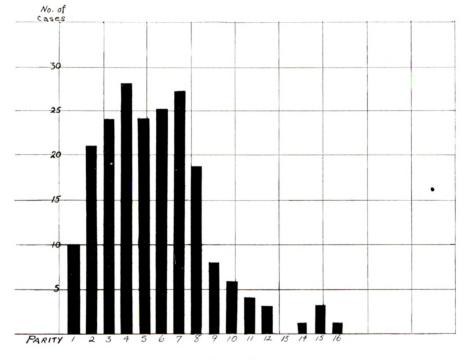


CHART II

Pregnancy does not tend to develop an immunity to carcinoma as shown by the fact that there was an average of over 5.4 pregnancies per patient in my series. Only ten were primiparas and 21 were para 11 whereas 159 were para 111 to para x (Chart II).

In all cases it is a question as to which precedes, the pregnancy or the cancer. The decision in each case must rest in great part on the extent of the growth and the month of pregnancy. For example, a small malignant polyp or bleeding ulcer on one lip which might be suspected from the Lugol's

cal experiment is often cited as evidence that pregnancy hastens the rate of growth. He marked the edge of a carcinoma of the cervix with a thread and found it extended two finger breadths in fourteen days. Ewing said, "Pregnancy has an unfavorable influence on the course of many uterine carcinomas not always apparent."

This seems to be borne out in one of my cases. She was treated with radium to the cervix and later a panhysterectomy was performed. There was no malignancy discoverable in the specimen and yet twelve months later the patient returned with in-

volvement of the pelvic nodes as proved by laparotomy. Thus it had spread rapidly during pregnancy and extended beyond the uterus. One of Sommer's cases was a woman, aged thirty-six, who was examined for pelvic pain in the eighth month. Nothing pathological was found. At term the growth was inoperable.

On the other hand, Siebold observed a spontaneous cure of genital carcinoma owing to a supervening pregnancy. Varniew in 1897 reported a case presenting an enormous carcinoma of the portio in a gravid woman. The following year another pregnancy occurred and death did not take place until October, 1900. Again there are case reports of second pregnancies after treating the cancer during the gravid state. Vitanza in 1898 did a high cervical amputation for carcinoma of the cervix during pregnancy. The patient was delivered later after forcible dilatation of the cervix and two years later was delivered again at eight months by a midwife. Vitanza found her free of cancer two years after that. His next case was operated on similarly in the third month. She was delivered at term of a 3,500 gram baby and of another two years later. In 1920 Siredey treated a pregnant woman for cancer of the cervix with radium. She aborted six months later. Two years after that she was again pregnant. The cervix remained clear and Siredey preformed a cesarean at term.

Because of a possibility that a pregnant woman has some cancer resisting hormone or hormone reaction I administered to some advanced carcinoma patients large doses of prolan and others I transfused with blood from pregnant women. Both groups of patients had severe reactions characterized by nausea, vomiting and mild to moderate shock, leading us to conclude that there may be some substance called forth in the body by pregnancy to resist tissue invasion (cancer).

Carcinoma has its effect on pregnancy. The inanition from cancer results in retarding the growth of the child. It may be a source of hemorrhage or infection. By

spread of infection or of neoplasm it increases the proportion of abortions. It may make the cervix rigid and obstruct delivery or make it friable and lead to rupture and death.

Symptoms. A patient usually pays no attention to a leukorrhea even after it becomes foul unless it is bloody. Thus sometimes she will miss what may be the first symptom of cancer. After a few months of amenorrhea a woman who realizes she is pregnant for the fifth or sixth time will go to her doctor at the first sign of bleeding from the vagina. Bleeding, therefore, is the most prominent and most common symptom and is usually heeded at once by the pregnant woman. The doctor thinking of the most common occurrence will treat her for a threatened abortion either with or without examining her. When we recall the fact that a carcinoma of the cervix occurs only once in 1,500 to 10,00 pregnancies we can see that he will rarely be wrong. But in that one case he may put the patient to bed to await developments. He will in this way lose weeks unless the hemorrhages become so profuse that he will examine the cervix both manually and visually. Then he will discover usually a growth which may need a biopsy to determine its nature. It is this type of cancer which gives a favorable prognosis today if operated on in that

If the hemorrhage occurs in the late months of pregnancy, placenta praevia is the first diagnosis to come to the mind of the obstetrician. Cases are on record in which cesarean sections were done because of this diagnosis unaware of the carcinoma of the cervix which was found only after the operation.

On the other hand, a woman may have a carcinoma of the cervix and bleed irregularly so that she has lost track of the menses. She will not realize that she actually has an amenorrhea and that the bleeding is due to a growth. Not realizing that she is pregnant, she will tell her doctor she has not missed a period. The doctor will find the carcinoma of the cervix and diagnose the enlargement of the womb as part of the growth. The result will be that the pregnancy will not be discovered until irradiation is given. If, however, the dictum is followed, that irradiation should be preceded by curettage as is done with radium there would be no question of a child injured by irradiation in such cases. In 1909 Williams wrote that pregnancy could not be diagnosed in some cases.

Table 1 •reveals the expected, namely that maternal mortality increases directly with the birth rate. This must be a warning, then, not to delay operation in order to obtain a living child. It may be pointed out that radical hysterectomy in expert hands has very little greater mortality than panhysterectomy before the seventh month and that one series of 11 cesarean sections followed by the Wertheim operation showed only one maternal death. This

TABLE I

	Total	Mothers Lived	Mortality per cent	Child Lived	Birth Rate per cent
Cesarean section	10	0	100	6	60
Ce arean section and abdominal hysterectomy	17	7	59	9	52
Cesarean section and supracervical hysterectomy	10	1	90	4	40
Cesarean section and Wertheim operation	11	10	9	4	36
Cesarean section and vaginal hysterectomy	2	τ	50	I	50
Total cesarean sections	50	19	60	24	48
Wertheim operation	42	26	38	I	organization of the state of th
( la - f	34	23	32		And
Abdominal hysterectomy after 7 mo.	2	0	100	J	
Vaginal hysterectomy	14	9	35	3	21
Vaginal hysterectomy post partum	11	4	63	4	36
Vaginal cesarean section and vaginal hysterectomy	4	2	50	2	50
Vaginal delivery	31	5	83	22	71
Cervical amputation	3	3	0	3	The second secon
Not classified	I	0	0		th man out an

Today we have the Friedman test which will prevent our overlooking a pregnancy if use is made of it.

In 1881 Thomas Spencer Wells reported the first successful hysterectomy by Freund's technique for carcinoma of the cervix in the gravid uterus. Thereupon Billroth, who had performed two vaginal hysterectomies for the same condition, wrote Wells: "Of what use are all our pains and art?" Wells answered: "May we not hopefully reply that if not invoked too late success may reward our pains and art." With improved surgical technique and earlier consultations in this group of patients an increased operability has been noted. Schweitzer found 9 operable out of II cases and obtained 5 five year cures among these 9. Weibel operated on 24 out of 26 cases.

may be interpreted to favor the theory that pregnancy holds the cancer in check. The release of this check may be assumed by the maternal mortality of 63 per cent in post partum vaginal hysterectomies as compared with 35 per cent when vaginal hysterectomy was done early in pregnancy.

Thirty-two patients were treated by irradiation alone (Table II). Fourteen mothers and II children lived, a maternal mortality and birth rate of 56 per cent and 37 per cent respectively. Besides 10 abortions or miscarriages in this group there were 2 microcephalics. One must consider these two failures.

Postconception irradiation before the seventh month as a cause of microcephaly has been confirmed by Goldstein and Murphy who investigated 106 women so treated. These women gave birth to 74

TABLE II

		Before Seventh Month				A CONTRACTOR OF THE PERSON OF	After Seventh Month			Totals All Months					
	Total	Mark	Maternal Mor- tality per cent	Child	Birth Rate per cent	Total	Mother Lived		Child Lived	Birth Rate per cent		Mother Lived			Birth Rate per cent
Irradiation ante partum or pre- operative Irradiation post	19	8	57	6	31	7	I	85	6	85	26	9	65	12	
partum or post- operative Irradiation ante and post par-	14	8	35	I	7	23	IO	56	16	69	37	18	51	17	
tum or pre- and post operative Months not given	18	8	55	11	60	5	1	80	2	40	23	9	60	13	And the same
Totals Irradiation alone from above	56	24	57	18	32	35	12	65	2.4	64	5 91	3 39	40 57	3 45	49.5
groups	26	11	60	9	34	6	3	50	2	30	32	14	59	11	37

TABLE III

	1111 11111 11111 1111 1111 1111 1111 1111	Ma	ternal R	esults	Child	Results		Mis- carriage	
•	Cases	Lived	Died	Mor- tality per cent	Lived	Died	Vaginal Births	and Abor- tions	
Irradiation alone	32	14	18	59	12	37	14	10	2 micro-
Irradiation then cesarean						and the second			cephalics
section	8	3	5	68	~	86			
Cesarean section then irra-		3	)	00	7	80		200	
diation	6	2	4	66	3	50			
Irradiation, cesarean sec-		_	-+		3	,,,			
tion then irradiation	5	2	3	60	4	80			
Irradiation, cesarean sec-			J		+				
tion then hysterectomy	7	2	5	71	4	58			
Cesarean section, hysterec-	1		,	/ /	-	, ,			
tomy and irradiation	7	2	5	71	6	86			
Cesarean section, Wertheim	1								
operation and irradiation	4	2	2	50	3	75			
Irradiation, cesarean sec-									
tion, hysterectomy and									
irradiation	2	0	2	100	0				
Irradiation and hysterec-									
tomy	2	0	2	100	1	50	I		
Hysterectomy then irradi-									
ation	9	6	3	33	2	22			
Irradiation, hysterectomy,									
then irradiation	I	I		0	1				
Irradiation then Wertheim									
operation	2	2		0	I		1		
Wertheim operation then									
irradiation	5	4	I	20	I		I		
Irradiation, Wertheim op-				The state of the s			T III		
eration then irradiation	1	I		0	0				

full term children, 38 of these children showed disturbances of anatomy or of function. Sixteen of these 38 were microcephalics and 2 others were mentally deficient without microcephaly.

Although many children have been reported normal in this series, one cannot be sure because they were reported soon after birth and microcephaly may not be recognized until the child is four years of age. Zimmermann reported such a child apparently normal until seven years old. This, then, together with the poor results are arguments against irradiation alone for cancer of the cervix during pregnancy.

Irradiation in combination with surgery follows the same rules as far as results go (Table III). When irradiation supplemented cesarean section alone or cesarean and hysterectomy it did not improve the results. When used with total hysterectomy or the Wertheim operation in the early months, the maternal mortality was 33 per cent and 20 per cent respectively—apparently a slight improvement over the operative treatment without irradiation only with the Wertheim operation.

The 2 cases that I have to present bring out some of the indications and objections to various forms of treatment.

## REPORT OF CASES

CASE I. An Italian woman, aged thirty-eight, was admitted to Mt. Sinai Hospital (under the care of Dr. Lesinger) on January 29, 1926. She was five months pregnant and para v. Onset ten days before admission with pains simulating labor pains. She said the "bag of water broke." Five days after this she noticed bleeding, scant at first but becoming more profuse each day. Examination revealed a uterus extending to the umbilicus. The movements of the child were felt. By rectal examination an irregular mass was felt protruding from the cervix. This was then confirmed by vaginal examination. The doctor stated that he thought it was a hand that protruded. She slept most of the night under ½ grain of morphine. She passed large clots of blood the next morning and by evening was bleeding profusely. She was then given I cc. of pituitrin. Bleeding became less. Because she had no pains she was discharged on the

fourth day with a diagnosis of "threatened abortion."

Ten days later she was readmitted because of severe bleeding. The same protruding mass was again felt. This time the cervix was visualized with a speculum and a polypous bleeding growth was seen. No fetal parts presented. This was diagnosed indurated cervical polyp and removed next day when it proved to be an epidermoid carcinoma. I was then consulted. I thought, inasmuch as it was a polypous growth, that I might hold it in check for two months. with radium treatment when the child could be removed by cesarean section. This was done. Radium therapy, 3,000 mg-hr., was given to the cervical canal. On April 20, 1926, Dr. Bubis did the cesarean section and immediate panhysterectomy and transfusion. The child died soon afterwards. No enlarged nodes were found in the pelvis. Dr. Kline reported that after careful examination and the taking of many sections there was no tumor tissue in the uterus or adnexa. There was an area of necrosis 3 mm. in diameter which was where the radium had been most effective. The patient made an uneventful recovery. She was discharged on the eighteenth postoperative day. She was then given roentgen therapy to the pelvis by Dr. H. Mahrer. His method consisted of treating four fields 15 X 15 cm. each, with 200 kv., 4 ma., for thirty minutes at 35 cm. distance, using a filter of 0.5 mm. copper and 1.0 mm. aluminum. The patient gained 30 pounds in the course of the ensuing year. She was readmitted to the hospital April 1, 1927. Five weeks previous to this admission she complained of pain in the back and right flank. She lost 8 pounds in five weeks. Dr. Bubis again did a laparotomy only to find a chain of hard nodes along the iliac vessels on each side. Dr. Kline reported metastatic carcinoma in lymph nodes.

This patient died in 1928, a little over two years after the onset of the carcinoma.

In retrospect we must appreciate that it must be usual to believe bleeding at the fifth month of pregnancy is due to threatened abortion from which carcinoma cannot be diagnosed without visualization and sometimes biopsy. We realize, too, that it is the practice of obstetricians to examine a pregnant woman as little as possible to avoid infection. Thirdly this is a striking instance of the ability of radium to destroy

the local growth and fail to destroy the growth already in the lymphatics. Therefore, it seems that just as the Wertheim operation has failed to cure those patients in whom the iliac nodes are involved, so, too, radium is suited for growths that are confined to the uterus. Fourthly, one must naturally raise the question—did the two months waiting for the child to become viable give opportunity for extension of the growth to the lymphatics, and would the patient have been cured if hysterectomy had been done as soon as the diagnosis was made? I feared more irradiation previous to cesarean section because of the irradiation effect on the child. I should be inclined under similar circumstances to act differently now. I would disregard the child and if preoperative radium treatment were given at all, operate two weeks later.

CASE II. A Polish woman, aged forty-two, para VIII, entered Mt. Sinai Hospital on Dr. Garber's service July 31, 1927. She was six months pregnant. Her seventh child had been born two years previously. She complained of bleeding for four months and abdominal pain since the afternoon preceding admission. She was anemic; red blood count 3,000,000, hemoglobin 60 per cent. Vaginal examination revealed an indurated papillomatous mass protruding from the cervix. Biopsy confirmed the diagnosis of epidermoid carcinoma. On August 3, a stillborn child was delivered by cesarean section. The pelvis was free of growth. This was followed five days later by heavy roentgen irradiation, as in the former case, and she was referred to me for the first time on August 22 for radium therapy. The growth occupying the cervix was 1½ inches in diameter. I applied 100 mg. in the cervical canal for twenty-four hours; October 28, 1927, 2,000 mg-hr. more. On July 23, 1928, the uterus was free but the mass was palpable high in pelvis. More roentgen irradiation given by Dr. Mahrer. The patient died early in 1929, a little less than two years after the onset.

From the history of this patient and the fact that she was not a very observing woman, it is fair to suppose that she had failed to take notice of a vaginal discharge before conception and that the bleeding in

the second month was from a carcinoma of more than two months' duration. Therefore, this was a preconception malignancy and well advanced after six months of pregnancy as evidenced by abdominal pain. It was a failure for irradiation.

Therefore, I believe we can formulate the treatment of carcinoma of the cervix depending on the stage of pregnancy as well as on the extent of the growth.

First: If the growth is operable and the child inviable, there is only the mother to consider. Delay may mean that the growth will advance from an operable to an inoperable one. It will diminish the chance of cure for the mother. As the carcinoma advances the chance of the child for life diminishes. Therefore, it is folly to wait for the child to become viable. Preoperative irradiation with radium must be incomplete as the uterine cavity cannot be irradiated thoroughly. Extensive and complete roentgen irradiation may make operation difficult, as well as cause abortion through a diseased cervix, and also deformities, especially microcephaly. Therefore inasmuch as one's greatest problem is with the patient, the inviable child should be disregarded in the treatment. A Wertheim operation is favored because the tissue planes are easily dissectible. Irradiation to the point of early abortion should be considered only in case the surgeon is not capable of the Wertheim operation. Irradiation to the cervix and supracervical hysterectomy should be discouraged just as much as in the nongravid carcinoma. In view of the poor results that occurred in postpartum carcinoma I believe that to leave any growth after removal of the fetus will mean that the restraining influence (fetus) will be removed and that will invite disaster.

Second: If the growth is operable and the child viable we prefer cesarean section and a Wertheim operation or panhysterectomy at once followed by postoperative irradiation as soon as the patient's condition warrants. There is not much choice, however, between cesarean section and

TABLE IV
LIST OF CASES IRRADIATED

Name	Mo.	Radiation Therapy (ap=ante partum)	0 .: p .:	Result on	
Name	Mo.	(pp=post partum)	Operative Procedure	Mother	Chile
Cotte, G. 1928	81/2	Radium, postoperative	Cesarean, total hysterectomy without removal of parametria	D.	D.
Döderlein, A. 1928	7	110 mg. radium bromide intravaginally for 24 hr. (ap)		D.	L.
Field, C. E.	?	Radium: (1) 100 mg. within cervix; scree rubber, 8 hr. crossfiring from a sacral pad 1.5 cm. felt 1.5 mm. rubber and 0.5 mr bomb 140 mg. screened with 1.5 mm. bra (3) 100 mg. standard screen within cervix.	containing 300 mg. screened with m. metal 16 hr.; (2) postcervical ss and 1.5 mm. hard rubber 8 hr.;	D.	L.
Hauch, E. 1927	8-9	Preoperative: radium; 3 tubes inserted total 125 mc-hr. with aluminum filter, rectum protected by lead sheet 2 mm. thick	Cesarean section	D.	L.
Same 1927	9	Radium: 3 tubes, 22 hr. 11 exposures x-ray. Radium amounts not given (pp)		D.	?
Same 1927	5	Postoperative: 21st day; 2 tubes radium for 20 hr. X-ray at 5½ weeks, radium at 8 weeks. Amounts not given	Cesarean section	I	4
Laquerriere, and Labelle	6	X-ray, 39 treatments, externally 2–8 min., then 13 cervical and 14 external. After delivery, 20 more treatments. No dosage amounts given (ap and pp)	•	D.	I
McGlinn, J. A.	3	2400 mg-hr. radium by capsule and needles into cervix (pp)	Aborted before treatment	D.	D.
Same 1927	9	36∞ mg-hr. X-ray 10 mo. later (ap and pp)	Cesarean section	D.	D.
Mundell, J. 1927	3	21∞ mg-hr. radium repeated in 2 mo. (ap)	Aborted	D.	D.
Schilling, N.	$4\frac{1}{2}$	Preoperative; local radium 100 mg. for 24 hr.	Cesarean section after 18 hr. labor; panhysterectomy	D.	D.
Gill, J. J. 1926	5	Postoperative; deep x-ray therapy	Hysterectomy and appendectomy	L.	D.
Vital, Aza 1917	6	Radium therapy over a period of 3 mo., 12,500 mg-hr.—50 mc-destroyed (ap)	Cesarean at term because of rigidity of cervix		L.
Strauss, A. Treated 1926	5	3000 mg-hr. radium intracervical (ap); postoperative x-ray therapy to pelvis, 200 kv. 4 ma. fiter 0.5 mm. Cu, 1 mm. (ap), 4 fields, 35 cm. distance	2 months later, cesarean section and immediate panhysterec- tomy; transfusion	D.	D.
Strauss, A. Treated 1927	6	Postoperative: heavy x-ray irradiation; 100 mg. radium, cervical canal, 24 hr. One month later, 2000 mg-hr.; 9 months later, mass palpable high in pelvis, roentgen irradiation given as in previous case	Stillborn child delivered by cesarean section	D.	D.

## TABLE IV—(Continued)

NI.	1	Radiation Therapy /ap=ante partum		Resul	t on
Name	Mo.	(pp=post partum)	Operative Procedure	Mother	Child
Audelbert and Galy 1928	9	Post partum: Nov. 19, 1925 (6 weeks) 10 needles 2 mg., 21.60 mc-destroyed Nov. 28 and Dec. 2 x-ray. Dec. 3, 8-36 mc-destroyed.		L.	L.
Roy 1926–28	9	Post partum: radium 167 mc-destroyed in 7 days	At term. Cesarean section. Subtotal hysterectomy	L.	L.
Roy 1926–28	4	At 4 months: 47 mc-destroyed in 5 days. At 6 months: 3.4 mc-destroyed in 2 days. Post partum: 1 month later 17 mc-destroyed in 3 days	Difficult forceps delivery; premature	D.	D.
Roy 1926–28	7	Radium 27 mc-destroyed in 5 days (ap)	Cesarean section at term and subtotal hysterectomy	D.	L.
Roy 1926–28	7	Radium 47 mc-destroyed in 5 days Radium 12 mc-destroyed in 5 days (ap)	Cesarean section and subtotal hysterectomy	L.	F
Karg-Carl 1928	6	Radium 3 times: Total 4000 mg-hr. Each about 1 month apart. Post partum further irradiation	Normal birth	D.	L.
Karg-Carl 1928	8	1320 mg-hr. in April (ap). Post partum irradiated twice	Normal birth June, 1925	L.	L.
Condamin, R.	2	125 mg. 48 hr. Radium bromide (ap)		D.	D.
Condamin, Voron and Molin	5	125 mg. 48 hr., Jan. 9 and Feb. 1, 3 weeks post partum, 125 mg. 48 hr. (ap and pp)	March 25 (somewhat premature) delivered by vagina	L.	D.
Neill, Wm. 1935	71	Dec. 15, 1926-4 glass radon capsules, 2.5 mc. implanted permanently in cervical stump. Dec. 18—1765 mc-hr. radon topically (ap)	Cesarean section; April, 1927, removed superficial metastatic nodule 1 cm. from right vaginal orfice with cautery	D.	L.
Neill, Wm. Jr. 1935	5	Topical application 3109 mc-hr. 10 months later, x-ray for a total of one s.E.D. over front and back of pelvis to establish artificial menopause (ap and pp)	Cesarean section	L.	L.
Neill, Wm. Jr.	3	Topical application against cervix, 36∞ mg-hr. in August, 1931 (ap)	Cesarean section in February, 1932	L.	L.
Neill, Wm. Jr. 1935	9	6 weeks postoperative: Topical applica- tion to cervix of 3000 mc-hr. and a series of deep x-ray. No change in 2 mo. Then 1 gold radon cap. 13.6 cm. permanently in cervix. 2 months later, 1000 mc-hr. against cervix	Cesarean section, June, 1931	D.	L.
Neill, Wm. Jr. 1935	1 hrs. after diagno- sis and birth	1½ years postoperative palliative x-ray. 1 week later 3000 mc-hr. radium irradiation	Cesarean section and supracervical hysterectomy	D.	L,

Table IV—(Continued)

	# P P P P P P P P P P P P P P P P P P P		-	Resul	t on
Name	Mo.	Radiation Therapy (ap=ante partum) pp=post partum)	Operative Procedure	Mother	Child
Neill, Wm. Jr. 1935	5	Oct. 1930 large mass removed-dull spoon curette. Topical application radium 3000 mc-hr. June, 1931, 1000 mc-hr. in vaginal vault for recurrent ulcer. Dec. 1933—1440 mc-hr.—recurrence (pp)	Spontaneous delivery August, 1930	D.	D.
Weibel, W. 1928	5	Artificial abortion with radium (ap)		L.	D.
Weibel, W. 1928	9	Radium (ap)	No operation	D.	?
Shoemaker, G. E. 1920	9	Postoperative radium	Postoperative radium  Removal of cancerous area with cautery and scissors, then forceps delivery and packing with iodoform gauze		D.
Kaplan, I. I.	3	3 doses of high voltage—50 per cent of a 25 per cent on posterior pelvis. Post part against cervix:—4300 mg-hr. over 4 days mg. into uterus, 2880 mg-hr. over 2 day x-ray to spleen—following 4 weeks more,	tum: "Colpostat 45 mg. radium 2. 2 days later radium sound—30 30 rs. Transfusion and high voltage	L.	D.
Morris, S. W.	6	2115 mg-hr. radium to cervix (ap)	3 days later, removal of uterus, tubes and ovaries	D.	D.
Morris, S. W.	3	Postoperative 12 days, 2000 mc-hr. radon to top of vagina (pp)	Panhysterectomy under spinal anesthesia	L.	D.
King, Gordon	9	Radium—14 days postoperative 4230 mg-hr. to cervix (pp)	Cesarean section and resection upper part of uterus	D.	L.
King, Gordon	7	Radium—12 days postoperative. Repeated twice per vagina: 4320 mg-hr. (pp)	Supravaginal hysterectomy	D.	D.
Mussey, Report of Mayo Clinic 1923	4	Radium and x-ray, postoperative	Total hysterectomy	D.	D.
Mussey, Report of Mayo Clinic 1923	3	Radium, postoperative	Total hysterectomy	D.	D.
Mussey, Report of Mayo Clinic 1923	4	Radium and x-ray (ap)		D.	D.
Nevinney, H.	9	Postoperative: secondary roentgen irradiation	Cesarean section followed by Freund-Wertheim; sacral anes- thesia, tutocain solution	D.	1
Cothala and Merat 1923	6	Radium refused for 1 month. Then 77 mg. radium bromide 24 hr. no reaction: 2 more hemorrhages 24 and 28 hr. later. Profuse discharge amniotic fluid (ap)	Cesarean section and total hysterectomy	D.	D.

## • Table IV—(Continued)

Name	Mo.	Radiation Therapy (ap=ante partum)	Out of Park	Result on		
1vame	IVIO.	(pp=post partum)	Operative Procedure	Mother	Child	
Brouha, M. and Gosselin, O. 1934	7	Radium: Tampons in posterior cul-de- sac, 13.33 mg. radium bromide in front of cervix filtered through 0.5 mm. plati- num, 1.25 mm. gold, 10 mm. rubber, 12 thicknesses gauze 4 days. 19.2 mc-de- stroyed; 15 days later condition same, 28.8 mc-destroyed in 8 days. Post- operative x-ray 1800 r in 30 treatments	Cesarean section 14 days later, followed by total hysterectomy	D.	D.	
Brouha, M. and Gosselin, O.	5	Same as above except radium in cervical canal and in posterior and lateral cul-desac. Cervix dilated and miscarriage (ap and pp)	Hysterectomy and deep x-ray therapy	L.	D.	
Masson, J. C.	7	Malignant growth treated with radium postoperative	Porro cesarean section one month after first seen	D.	L.	
Behney, C. A. 1930 (Keene)	6	Cautery amputation of cervix, 100 mg. radium 36 hr.: 2 months later delivered of apparently normal child. Then 100 mg. 36 hr. more	Child a microcephalic	L.	Ì.	
Keene, F. E.	31-4	2 weeks postoperative: wide cauterization of cervix, 2400 mg-hr. radium	Supravaginal hysterectomy and bilateral salpingo-oöphorectomy as a primary procedure	L.	D.	
De Nabias	8	Postoperative: 4 tubes radium in cervix—each 10 mg. filtered through 1 mm. platinum for 5 days. Then 3 tubes through vagina. 7200 mg-hr. or 54-60 mc-destroyed	Median laparotomy—difficult to exterorize uterus—living child. Round and tubo-ovarian ligaments sectioned. Uterine arteries ligated; cervix sectioned	L.	L.	
De Nabias 1925	4	4 applications: 4320 mg-hr. or 32 mc- destroyed. Postoperative 54 mc-de- stroyed in 12 days (ap)	Cesarean section at 8½ months followed by subtotal hysterectomy	L.	L.	
Zimmermann, R.	6	Post partum mesothorium and x-ray	Spontaneous miscarriage through growth	D.	D.	
Zimmermann, R. 1928	6	Mesothorium intracervical 100 mg. Intravaginal 50 mg. for 24 hours—3600 mg-hr. Postoperative x-ray. Also 100 mg. mesothorium intravaginally	Total hysterectomy, cesarean section at 7 mo.	D.	7	
Zimmermann, R.	7	109.6 mg. mesothorium 24 hr. in crater. Post partum roentgen irradiation (ap and pp)	Miscarriage at 8 months	L.	D.	
Zimmermann, R. 1920	5	Mesothorium 3 times at 6 week intervals, twice 100 mg. intracervical and 50 mg. intravaginal for 24 hr.—3 times, total 4390 mg-hr. 12 weeks post partum: 109.6 mg. 24 hr. mesothorium	Normal delivery. Microcephalic	L.	L.	
Paroli, G.	3	Radium element—5760 mg-hr. in 3 weeks (ap)	Cesarean section	L.	L.	
Siredey, and Gagey 1920 & 1924	8-10 weeks	Intracervical 15.7 mc-destroyed (ap)	Aborted 2 years later a cesarean section	L.	D. L.	

Table IV—(Continued)

		Radiation Therapy / ap = ante partum		Result on		
Name	Mo.	(ap=ante partum)	Operative Procedure	Mother	Child	
Hartmann, and Fabre	4	11/24/22—cervical radium—25.92 mc- destroyed. 11/25/23—7.04 mc-de- stroyed (ap and pp)	3/11/23—cesarean section fol- lowed by supravaginal	D.	I	
Philipp, E.	4	April 1924—118 mg. 30 hr. (in cervix, 1 tube 40 mg. and 1 of 26 mg. in front of cervix, 2 tubes 26 mg.). Repeated in 9 days. Total—7000 mg-hr.	Aborted 2½ months later	I	D.	
Pouey, H. 1927	61/2	10/3/23—Radium. In 3 days total 28.4 mc-destroyed. One day rest then in 4 days 14.4 mc-destroyed. Total—43.2 mc-destroyed. 1/10/24—26.4 mc-destroyed rectal necrosis from radium (ap and pp)	Delivered Nov. 28, 1923; 18 days before term, in labor for 20 hr.	L.	L.	
Bailey, and Bagg	$6\frac{1}{2}$	Radium emanation—"Bare tubes," and platinum tube radium 2356 mc-hr. Next day, 960 mc-hr. bomb applicator to cervix; 297 mc-hr. "Bare tubes" to cervix (ap)	Eclampsia—cesarean section—6 weeks after radium	D.	D.	
Favreau, M. Lamelin, P.	4	2/10/26—4800 mg-hr. radium. 1/27—radium, 20 mg. times 15 days. 0.5 mm. lead, vaginally at 1.5 cm. from vault (ap)	6/10/26—delivered of living child. 10/26 hysterectomy	D.	I	
Metzger 1923	3	Radium 18 mc-destroyed. Cancer disappeared after 5 weeks (ap)	Delivered at term by incision in rigid cervix and by forceps	D.	?	
Peralta 1927	7	July 24. Ra bromide—100 mg. for 24 hr. Aug. 8—100 mg. for 24 hr. 1 mo. post-operative—deep therapy x-ray repeated 2 days later 3 hours (ap and pp)	Aug. 19—fetus died in utero. Aug. severe uterine contractions, Wertheim without cesarean sec- tion	L.	D.	
Peralta 1927	9	6 weeks postoperative deep therapy x-ray repeated 1 mo. later	At term Wertheim and cesarean section	L.	L.	
Heraud, C.	6	11/25/32—radium 25 mc-destroyed (ap)	Delivered at term, preliminary ligation of hypogastric arteries, then Wertheim	L.	L.	
Lukas, Josef 1924	6	At 6½ mo. radium—20 mg.+10+10+10 ×70 hr.: total 3500 mg-hr. 3 mo. later, 4×6 mm. ulcer, leukoplakia of post. lip then given—10 mg. intrauterine, 20 mg. in cervix, 10 mg. across cervix, 10 mg. in each vault total, 3500 mg-hr. (ap and pp)	(Dilation and curettage in May, 1932.) Delivered of premature child at $7\frac{1}{2}$ mo.	L.	L.	
Peter, R. 1935	9	Postoperative x-ray therapy	Vaginal hysterectomy and de- livery. Wertheim	L.	L.	
Peter, R.	8	Radium and x-ray administered in 7th mo. Repeated postoperative (ap and pp)	Membranes ruptured 15th day after treatment. Cesarean	D.	L.	
Lacomme, M. Pallud, O. 1936	?	Radium—aborted 2 mo. later	Delivered at term of second child (pregnant again 1 year later)	L.	O.	
Wollebeck 1935	9	Postoperative x-ray	Cesarean section, complete hysterectomy	L.	L.	

## TABLE IV—(Continued)

Name	Mo.	Radiation Therapy (ap-ante partum)	On-red : P 3	Resul	t on
TARMS	1710.	pp=post partum)	Operative Procedure	Mother	Child
Pomeroy, L. A. 1936	41/2	Postoperative: x-ray 32 treatments, 4 fields each received 2400 r. total—9600 r. Radium—I long tube 83 mc. screened, 1.5 aluminum 5 mm. silver, I mm. brass applied so as to occupy entire length of uterine canal—34 hours—2490 mc-hr. Cervical implantations 8 mc. gold—2112 mc. total radium—4602 mc-hr.	Abdominal hysterotomy	L	D.
Rheuter 1922	9	Postoperative—radium therapy—8/22/ 22 and 9/26/22. No dosage given	Cervical embryotomy	D.	D.
Heuze 1929	?	Postoperative—1 year, radium therapy. No dosage given	Cesarean section at term	D.	L.
Heuze 1929	9	Postoperative—radium no dosage given	Cesarean section at term	D.	L.
Heuze 1929	3	Radium at 3rd month, no dosage given (ap)	Cesarean section at term	L.	L.
Bottaro and Bengoa 1919	6	Preoperative radium. Postoperative x-ray. 9/1/17—50 mg. 24 hr. 48.5 mc-destroyed. 9/9/17 and 9/22 and 10/5 and 10/16 with total 24 mc-destroyed	Cesarean section at term	L.	L.
Addessi, G.	8	Postoperative x-ray; no dosage given	Total hysterectomy and adnex- otomy	L.	L.
Roche 1921	5	Radium—110 mc. in cervical growth for 44 hr. 19.35 mc-destroyed (ap)	Delivered at term	.5	L.
De Rouville	5	100 mg. in vagina 9.6 mc-destroyed (ap)	Miscarriage	L.	D.
Biro, S. 1918	9	5 months postoperative 183 mg. 24 hr.	Cesarean and Wertheim	D.	?
Biro 1922	9	17 days post partum 84 mg. 20 hr. in vagina. 1 mo. later, 70 mg. 24 hr. X2	Cesarean and Wertheim	L.	L.
Biro 1922	5	42nd day 84 mg. 24 hr. in vagina 2016 mg-hr. 6 weeks later 70 mg. 24 hr. in vagina 1680 mg-hr. 9 weeks later 84 mg. 24 hr. in vagina 2016 mg-hr. (pp)	Wertheim after preparation of vaginal cuff	L.	
Biro 1922	8	3 weeks post partum 84 mg. 24 hr. 2016 mg-hr. 1 month later 98 mg. 24 hr. 2352 mg-hr. 3 months later 70 mg.×24 hr. 1680 mg-hr.	Cesarean and Wertheim	L.	L.
Biro 1922	3	15th day 84 mg.×24 hr. 2016 mg-hr. 1 mo. later 70 mg.×24 hr. 1680 mg-hr. 3 mo. later 70 mg.×24 hr. 1680 mg-hr. (pp)	Vaginal hysterectomy	L.	
Biro 1925	4	On 19th day x-ray series (5 fields) 2 days later radium 70 mg. 24 hr. 1 month later 84 mg. 24 hr. 2 days later x-ray series (5 fields) (pp)	Wertheim	L.	

Table 4 (Continued)

Name	Mo.	Radiation Therapy (ap=ante partum)	Oi Pi	Result on	
Name	IVIO,	(pp=post partum)	Operative Procedure	Mother	Child
Biro 1925	4	37th day 84 mg. 24 hr. 2 months later 98 mg. 24 hr. (pp)	Wertheim	L.	ethiologia hit said it commission acceptation
Biro 1925	5	12th day post partum x-ray series; 6 weeks later repeated	Wertheim	D.	MOTERATE PLANT AND PLANT SECURITY AND
Nielsen 1916	6	Ante partum radium. 4/23/1916 to July 1, 2480 mc-hr. of which 1512 mc-hr. intracervical; post partum 3768 mc-hr.	Spontaneous delivery	D.	L.
Nielsen 1929		Vaginal applications 5040 mc-hr. parametria free clinically (ap and pp)	Cesarcan. Parametrium rigid at operation. Recurrence treated 11 mo. later	L.	L.
Commandeur 1925	81/2	15 days postoperative 100 mg. in cervical stump, 75 mg. in vagina 72 hrs.	Cesarean and Porro section	D.	L.

irradiation or cesarean section and operaion. Much will depend on the operator. The prognosis is poor—60 to 70 per cent mortality.

Third: When the growth is inoperable and the child viable then we should explain the condition to the husband to obtain permission for a cesarean section. Because of the dangers of rupture of the uterus, or a tear starting in the cervix and extending into the uterus or of hemorrhage or of sepsis, in these days of asepsis one should never wait to deliver the child per vaginam. With the uterus emptied, the mother should be treated as soon as her condition warrants by intrauterine radium and deep roentgen therapy. The maternal mortality here is about 65 per cent.

Fourth: If the growth is inoperable and the child inviable the chance of saving the mother by irradiation without emptying the uterus is nil. It must be admitted that unless one believes that pregnancy will check the growth the irradiation should be as thorough as in the nonpregnant. No one would be content with cervical irradiation alone in the latter. If radium is applied intrauterinely, abortion will probably follow. Therefore, if treated thoroughly enough the products of conception will be lost. The fetus should not be considered.

Here, then, we are impressed by the aid irradiation gives when the surgeon is prevented from operating or when surgery is contraindicated. Because of the fetus or child it cannot be used so thoroughly nor so efficiently as in the nongravid. However, it becomes a method second to surgery, and always as an adjunct to surgery in any of the four groups. Nevertheless cures have been obtained with irradiation and cesarean section and irradiation should be used, especially when the choice of the patient requires it. By this method the birthrate has been high. The dangers to the child by irradiation must be remembered.

## SUMMARY

- 1. Carcinoma of the cervix during pregnancy is rare.
- 2. The effect of pregnancy on the growth of the cancer and the effect of the growth on pregnancy have been discussed.
- 3. The usual main symptom which brings the patient to the doctor is hemorrhage.
- 4. The diagnosis can be made only by visualizing the cervix.
- 5. Prognosis is good when the condition is operable.
- 6. Operability is higher in this group than in the nonpregnant.

- 7. The treatment depends on the operability of the growth and the stage of pregnancy.
  - a. If the growth is operable and the child inviable, disregard the child and remove all pelvic organs. Then administer postoperative irradiation.
  - b. If the growth is operable and the child viable precede the operation with an abdominal cesarean section.
  - c. If the growth is inoperable and the child viable perform an abdominal cesarean section and use postoperative irradiation.
  - d. If the growth is inoperable and the child inviable, the choice rests with the family. Preference should be given to thorough irradiation to cause abortion, and then further irradiation as indicated. If pregnancy is in later months irradiate and perform cesarean section as soon as the child is viable. Then irradiate again if necessary.
- 8. Delivery should not be allowed through the cervix.
- 9. Any restriction in the treatment of the patient in order to save the offspring will be at the expense of the mother.
- 10. The higher the birth rate in any given group in this series, the higher the maternal mortality usually is.
- 11. After the seventh month of pregnancy irradiation does not improve results either with or without surgery.
- 12. Before the seventh month irradiation following operation slightly improves maternal results.
- 13. Radical operation should not be delayed for irradiation.\*
  - \* For discussion see page 571.

#### REFERENCES

- 1. Bubis, J. L. Puerperal Gynecology. William Wood & Co., Baltimore, 1935, p. 74.
- Ewing, J. Neoplastic Diseases. Lea & Febiger, Philadelphia, 1919.
- 3. Murphy, D. P., and Goldstein, L. Etiology of the ill-health of children born after maternal pelvic irradiation. I. Unhealthy children born after preconception pelvic irradiation. Am. J. Roentgenol. & Rad. Therapy, 1929, 22, 207-219.
- 4. Goldstein, L., and Murphy, D. P. Etiology of the ill-health of children born after maternal pelvic irradiation. II. Defective children born after postconception pelvic irradiation. Am. J. Roentgenol. & Rad. Therapy, 1929, 22, 322-331.
- HIRST, B. C. Incidence of cancer of cervix in pregnancy. New York State J. Med., 1923, 23, 300-303.
- 6. Mussey, R. D. Quoted by Hirst, ref. 5.
- 7. Pomerov, L. A. Unpublished case, University Hospital, Cleveland, Ohio.
- 8. Schweitzer, B. Pregnancy with cancer of uterus. Zentralbl. f. Gynāk., 1923, 47, 657-667.
- 9. SIREDEY. Bull. Soc. d'obst. et de gynéc. de Par., 1923, 112.
- IO. SOMMER, K. Effect of pregnancy on cancer. Zentralbl. f. Gynäk., 1925, 49, 758-762.
- II. VITANZA, R. Arch. di ostet. e ginec., 1892, 5, 670-692.
- 12. Weibel, W. Fünf und zwanzig Jahre "Wertheimscher" Carcinomoperation. Arch. f. Gynäk., 1928, 135, 1-57.
- 13. Walls. Caesarean section and Wertheim's hysterectomy for pregnancy with carcinoma of the cervix and double papillomatous ovarian cysts (exhibition of specimen). J. Obst. & Gynaec. Brit. Emp., 1914, 26, 64.
- 14. WILLIAMS, J. T. Cancer of cervix complicating pregnancy. Boston M. & S. J., 1909, 160, 669–677.
- 15. ZIMMERMANN, ROBERT. Cervixcarcinom und Schwangerschaft, unter Berücksichtigung der Frage einer Strahlenschädigung der Frucht. Strahlentherapie, 1928, 29, 108-121.
- 16. ZWEIFEL, P., and PAYR, E., editors. Die Klinik der Bösartigen Geschwülste. Band III. S. Hirzel, Leipzig, 1927, p. 243.



# A FURTHER REPORT ON THE RADIUM TREATMENT OF CARCINOMA OF THE CERVIX UTERI

## ONE HUNDRED AND THIRTY-FIVE ADDITIONAL CASES WITH FIVE YEAR FOLLOW-UP\*

By H. C. PITTS, M.D., F.A.C.S., and G. W. WATERMAN, M.D., F.A.C.S. PROVIDENCE, RHODE ISLAND

IN A PREVIOUS publication, we reported a five year follow-up on 173 cases of cancer of the cervix treated by means of long platinum filtered radium needles of low intensity acting over a long time interval. Today we wish to report a five year follow-up on 135 additional cases treated in 1931, 1932, and 1933 by the same method, and to bring out again the advantages of the method as well as to show that in our hands there has been no higher immediate mortality or incidence of complication than is experienced in other forms of radiation therapy for cancer of the cervix.

We wish it understood that these are chronologically consecutive cases as they come into the clinic. The total 173 for the first report, and the 135 for this report, represent all cases seen at the clinic, whether treated or untreated subsequently by us, or whether sent to our clinic after unsuccessful treatment elsewhere. The totals also include all cervical stump cases.

The 173, and the 135 then, are the absolute figures required in reporting such series. If the number of cases untreated because too advanced or for other causes is deducted from the absolute figure, the *relative* figure or the number of cases actually treated is obtained. This is 173 minus 8, or 165 for the first series; and 135 minus 11, or 124 for the present series. The absolute figure for the two groups is 308. The relative figure is 289, i.e. 308 minus 19.

If the cases of cancer of the cervical stump are not included, it being felt by some writers that they present a special problem and consequently should be set aside in a group by themselves, then the relative figure becomes 289 minus 11, or 278, there being 11 cases of cancer of the cervical stump included in this series.

Finally, if it is desired to show the relative results on cases treated primarily by this method and for which we have been responsible throughout, it is necessary to deduct the number of cases which have come to us after being treated elsewhere There have been 14 such cases.

### THE METHOD

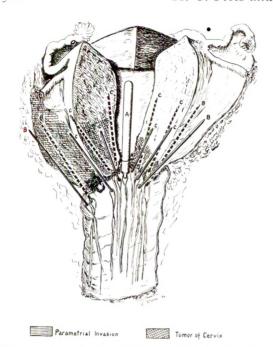
There has been no change in the method as reported and described two years ago except that roentgen therapy has been used somewhat more freely. It is not felt that the roentgen therapy has materially affected the five year results as the dosages employed in those years would hardly be considered adequate today. By the use of the interstitial radium needles implanted into the paracervical and parametrial tissues together with the use of a capsule in the cervical canal, a dosage of 3,300 mghr. in the cervical canal, and of about 6,000 mg-hr. in the parametrium is obtained. The distribution of the needles is illustrated in the accompanying figures. But one application is planned and this lasts six or seven days, the radium, of course, being undisturbed during this time.

## RESULTS

The results of treatment of 135 additional cases are shown in the accompanying charts. A comparison of results obtained in the different clinical stages shows very

<sup>&</sup>lt;sup>1</sup> Pitts, H. C., and Waterman, G. W. Treatment of cancer of the cervix uteri at the Rhode Island Hospital. Surg., Gynec. & Obst., 1937, 64, 30-38.

<sup>\*</sup> Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.



Figs. 1-3. A, 20 mg. platinum filtered tube; B, 3 mg. platinum needles; C, 2 mg. platinum needles. (Courtesy of Surgery, Gynecology and Obstetrics.)
Fig. 1. Lined area indicates advancing parametrial invasion; cross-hatched area, cervical tumor; dotted needles are posterior to midline of cervix.

little difference from the results obtained in the previously reported 173 cases treated by the interstitial method in spite of the fact that more roentgen therapy was used in these last 135 cases. Of particular

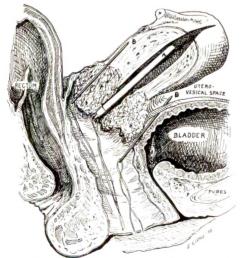


Fig. 2. Method of inserting needles anteriorly and posteriorly.

interest are the survival rates in Stage III (Schmitz) cases, that for 1926–1930 being 18 out of 62, or 29 per cent; that for 1931-1933 being 16 out of 48 cases, or 33.3 per cent. A comparison with a series of Stage III cases which we treated between 1921-1925 by a method of intracavitary application of radium, where only 6 cases out of 43 survived five years (14 per cent) shows that the survival rate for this stage has been raised over 100 per cent. The authors feel that, while it may be difficult or impossible to compare results from different clinics by clinical stages, it is possible to compare results in one clinic where the classifving into stages is done by two men working together with a common idea. We feel that our classification of Stage III cases has been consistent and reasonably dependable throughout these series. In the first

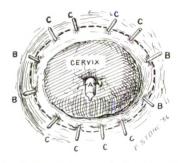


Fig. 3. Lined area shows cervical tumor; dotted line shows area of paracervical invasion.

series (1921–1925) the percentage of Stage III cases to the total was 43:120, or 35 per cent; in the second series (1926–1930) the percentage of Stage III cases was 62:173, or 35.8 per cent; and in the third series the percentage of Stage III cases was 45:135, or 33.3 per cent.

The ability to deliver approximately 6,000 mg-hr. of gamma radiation into the parametrial and paracervical tissues, in addition to the usual 3,000 mg-hr. in the cervical canal without tissue breakdown or other serious complications, is believed to be the telling factor in producing the good results by this method in the Stage III cases.

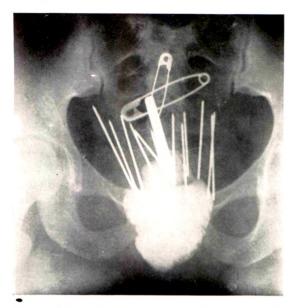


Fig. 4. Roentgenogram showing needles and capsule in place. Dense area shows iodoform packing in vagina. (Courtesy of Surgery, Gynecology and Obstetrics.)

## COMPLICATIONS

The insertion of long needles through the vaginal fornices into the parametria in cases of advanced and broken down cervical cancer would seem to invite disaster from infection—parametritis—peritonitis, etc. The danger of fistula formation has likewise been advanced as an objection to the method. We have now actually treated to December 31, 1938, 480 cases in our clinic. Complications of (1) immediate

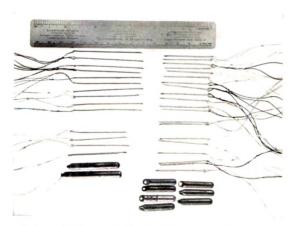


Fig. 5. Radium available. (Courtesy of Surgery, Gynecology and Obstetrics.)

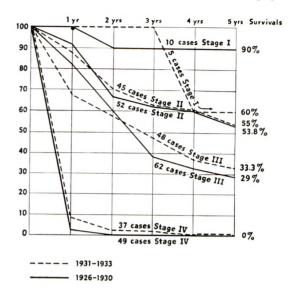


Chart I. Showing comparison between two series treated by the interstitial method. Note that the curves for Stage II and for Stage III run about parallel with slight advantage for the 1931–1933 series.

mortality and (2) fistula formation are as follows.

In 505 cases seen in the clinic, 25 were too advanced to treat; 480 cases were actually treated. Of these 13 cases died before leaving the hospital, a gross mortality of 2.7 per cent. Two of these patients died of massive hemorrhage, one five days after removal of the needles, one eighteen days after. As both of the patients had bled

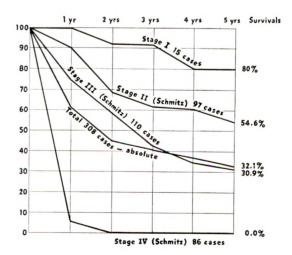


CHART II. Showing combined results of two series: 1926–1930 and 1931–1933.

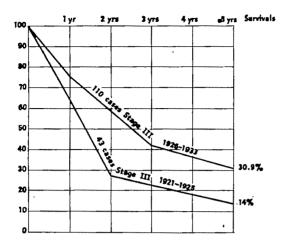


CHART III. Comparison in the results between Stage III cases treated by the interstitial method (110 cases 1926–1933) and Stage III cases (43 cases) treated by other methods (1921–1925), showing an improvement of more than 100 per cent or twice as many survivors by the interstitial method.

quite freely on admission it was not felt that the treatment had much to do with the hemorrhage. Two patients died of pulmonary embolism, one of coronary thrombosis, one of pyelonephritis sixteen days after treatment proved by autopsy with no local infection in pelvis and no peritonitis. One patient died fifty-three days after treatment of bilateral hydronephrosis and uremia and one died thirty minutes after treatment, an anesthetic death. This patient had advanced cancer and in addition had a bad heart and was diabetic. Five patients died of infection of these one had a thrombophlebitis and septicemia and died thirty-two days after treatment, 2 had peritonitis and 2 sepsis seven and twenty days after treatment. These last 5 cases were all Stage IV cases, probably would have been better not treated, and probably would have succumbed to any method of interference. However, 5 patients out of 480 who died of sepsis gives a corrected mortality of slightly over I per cent which might be charged against the method.

## INCIDENCE OF FISTULA

We give these figures not because we feel that they are any gauge of the de-

structiveness of radium treatment, because there is a definite incidence of fistulae in cervical cancer treated or untreated, but because fistula formation is an objective phenomenon, which when it develops after treatment, quite naturally in the mind of the uninitiated must have arisen from the treatment. We all know how close the cervix lies to bladder and rectum, how advanced cervical cancer often actually invades bladder and rectal walls. In the natural course of the disease many breakdowns of bladder and rectal wall occur. Of course an effective dose of radium applied against or into a cancer invading bladder wall may easily break down the cancer tissue and leave a fistula. We have always felt, however, that interstitial needles of low intensity placed in the vesicovaginal) or rectovaginal septum were far less likely to cause breakdown and fistula formation than were larger plaques, bombs, or applicators of greater intensity. We offer then this actual experience for what it may be

TABLE I
Results: 5 Year Survivals Interstitial Method

	-				
1931-33		cases—absolute			32.6%
	124	cases—relative	44	survivals	35.4%
Stage 1	5	cases	3	survivals	60.0%
Stage 11	45	cases	25	survivals	55.0%
Stage III	48	cases	16	survivals	33.3%
Stage IV	37	cases	0	survivals	0.0%
1926–30	173	cases—absolute	55	survivals	31.8%
, ,		cases-relative			35.7%
Stage 1	IQ	cases	9	survivals	90.0%
Stage 11	52	cases	28	survivals.	53.8%
Stage III	62	cases	18	survivals	29.8%
Stage IV	49	cases	0	survivals	0.0%
1926-33	308	cases—absolute	99	survivals	32.1%
•	289	cases-relative	99	survivals	34.2%
Stage 1	15	cases	12	survivals	80.0%
Stage 11	97	cases	53	survivals	54.6%
Stage III	110	cases	34	survivals	30.9%
Stage IV	86	cases	0	survivals	0.0%

## Results: 5 Year Survivals Other Methods

1921-25	120 cases-	–absolute 24	survivals	20.0%
Stage 1	4 cases		survivals	
Stage 11	19 cases	12	survivals	63.1%
Stage III	43 cases		survivals	
Stage IV	54 cases	2	survivals	3.7%

worth. We feel that these figures are quite accurate. We have an excellent follow-up service and get word of what happens to our patients in about 98 per cent of all cases.

In a total series of 480 cases treated (1926–1938 inclusive) 38, or 7.9 per cent, developed fistula: 13 cases had vesicovaginal fistulas alone, 13 cases had rectovaginal fistulas alone, 11 cases had both vesicovaginal and rectovaginal fistulas and 1 case had an ileovaginal fistula. Six of the 38 cases were untreated or developed fistula following hysterectomy performed because they were not doing well and surgery seemed to offer some hope. Six cases closed spontaneously or were closed by operation.

#### CONCLUSIONS

We do not feel that interstitial irradiation as employed in this series is excessively dangerous or productive of high immediate mortality from sepsis or that the incidence of fistula formation is more than naturally occurs or would occur with any method of radium treatment.

We have given five year results on a new group of 135 cases seen and examined at our clinic at the Rhode Island Hospital. The good five year survival rate of a previously reported series of 173 cases is here repeated. Charts are shown illustrating the curve of survival rates for each group and stage for each of the five years.

Special attention is called to the increased survival rate in Stage III cases over that for the same stage treated by other methods in our own clinic.

We have used the absolute figure of 308 in calculating survival percentages in these charts. If 19 cases too advanced to treat, 11 cervical stump cases, and 14 cases treated elsewhere with radium and/or roentgen irradiation before coming to us, are deducted from the 308, we get a relative figure of 264 which represents cases of carcinoma of the cervix actually treated primarily by our method. If we deduct from our total survival figure of 99, the 2 surviv-

als in the group of cases of the cervical stump and the 2 survivals in the group of those treated elsewhere, we obtain a figure of 95 survivals of cases treated primarily by our method.

The relative survival rate is, with these deductions, 95:264, or 36 per cent.

DISCUSSION ON PAPERS OF DRS. TAUSSIG, FRICKE AND BOWING, STRAUSS, AND PITTS AND WATERMAN

DR. A. N. ARNESON, St. Louis, Mo. The symposium presented this morning has brought to our attention some of the most important problems in cervical cancer. Carcinoma of the cervix complicated by pregnancy is a relatively rare condition. Few individuals have had the opportunity to see more than one or two such patients. The diagnosis of cervical cancer with pregnancy presents an emergency, and it is essential that we become familiar with the experience of others. Carcinoma of the cervical stump always presents a difficult problem in treatment. Dr. Fricke has reviewed statistics published for cancer of the cervical stump, and it has been very gratifying to hear the improvement in clinical results reported for different methods of treatment.

Two of the papers presented this morning have described methods that represent something of a departure from more conventional methods of treatment for primary carcinoma of the cervix. Each method is used in the attempt to increase the percentage of cures by control of the tumor within a greater volume of tissue. Dr. Taussig's method, for example, presents a technique for surgical removal of lymph node metastases beyond the effect of radium applied within the uterus and in the vagina. Dr. Waterman and Dr. Pitts have attempted to deliver greater doses of radiation to those regions by inserting radium needles into the paracervical and parametrial tissues.

For some time there has been fear of severe reactions following the use of interstitial irradiation in cervical cancer, and fear of introducing infection by the insertion of needles. Dr. Waterman has presented additional data to show that they have not had a high incidence of sequelae following their technique of treatment, and they have certainly obtained clinical results that are among the best reported here or abroad.

Following an earlier publication by Dr. Pitts and Dr. Waterman we began about three years ago to use radium needles in some patients. The method has not yet been applied to all cases as a routine procedure. At first we began cautiously with an empirical type of treatment. At a later date the attempt was made to work out a more elaborate scheme for delivering a predetermined dose. It is obvious that it is not always possible to calculate tissue doses very accurately, but little by little the method has been used in an increasing percentage of patients. Sufficient time has not elapsed for us to say anything about permanent cures, but it can be said that we have obtained very satisfactory results. In many instances a better result has been obtained than might have been expected from radium applied only in the uterus and in the vagina.

One might expect an improvement in clinical results from the use of needles due to the multiple sources of radium distributed widely throughout the tumor-bearing region. Due to the contribution from the different sources no single one need be used for a dose apt to produce extensive necrosis. By that means a more uniform distribution of radiation can be obtained with less discrepancy between the minimum dose reaching some parts of the tumor and the maximum amount falling on other points. If variations in the distribution of specified doses can be lessened, it is also possible to increase the minimum quantity delivered to the tumor. For the technique in question the improvement is chiefly in the parametrial regions. Any attempt to increase the percentage of cures obtained in the treatment of cervical cancer must have as its aim a method that will result in improvement in the parametrial dose.

In our experience the use of interstitial irradiation has not been followed by serious complications. Among a total of more than 50 patients bleeding has occurred upon removal of the needles in about 4 or 5 instances. The appearance of bleeding with removal would indicate that it was due to erosion into a blood vessel during the time the needle was in place rather than to puncture by insertion. Fever has been of no importance except in a few patients with badly infected lesions, and in all probability needles should not have been used in those individuals. In 2 instances we have had a mortality that appeared to be due to treatment. Both patients had extensive lesions that

were unquestionably over-irradiated. Uremia occurred in each instance, and the patients died within a short time after treatment.

There are two questions I should like to ask Dr. Waterman. It has been our practice to bury the needles beneath the mucous membrane. If they are not pushed in that deeply, short sources are apt to fall out of place. At the same time a needle inserted in that manner may be difficult to remove due to the fact that the head may not be in line with the suture protruding through the puncture wound. In some instances we have had to cut down on the mucous membrane with great risk of severing the suture. I should like to ask Dr. Waterman if he, too, has had that difficulty. It may be that we have used insufficient vaginal packing, and with a firmer gauze support it may not be necessary to bury the needle completely.

The second question I would like to ask is whether or not he has ever lost a needle and if he has, what success he had in recovering it. That such an accident might occur has been our greatest fear.

DR. W. H. WEHR, Buffalo, N. Y. I would like to comment briefly on our experience with carcinoma of the cervix associated with pregnancy,—very limited, of course, but in the period of 1930 to 1933 there were admitted to the clinic almost 700 patients suffering from carcinoma of the cervix and only 2 of these were pregnant at the time of admission. Both patients were three months pregnant; the first one showed a lesion of the posterior fornix and adjacent vaginal wall, and while a rather small lesion, the anatomic extent of it would definitely put it into a Schmitz Stage II.

This lesion was implanted with gold seeds for a total of 1,320 millicurie-hours and we hoped that this would hold the growth in check until the patient was delivered and following delivery that this patient would be thoroughly treated with interstitial, intercavitary and external irradiation by means of high voltage roentgen rays.

Withir six or eight weeks following the implantation of seeds, the lesion completely disappeared.

The patient was delivered in the normal manner and is now six years and seven months past the date of her treatment and there has been no recurrence and, needless to say, there has been no further treatment given.

The second patient also had a Stage II lesion, much more extensive, involving the entire cervix with infiltration of all fornices but no definite infiltration of either parametria.

This lesion was implanted with a total of 2,320 mc-hr. and the bleeding and discharge ceased. At the time of the delivery, this patient had a cesarean section. The surgeon reported to us at that time that there was no evidence of recurrence. However, within a month there was a definite recurrence and this patient was treated in the usual manner at our clinic,—with interstitial radon, intercavitary radium and high voltage roentgen rays.

There was some palliation but the patient succumbed in one year and three months.

In addition to these 2 patients there were 16 others who had carcinoma of the cervix and pregnancy but had not reported to the clinic until after delivery or until after miscarriage. Six of the patients were admitted following miscarriage, all of whom gave a history of bloody and watery discharge during their period of pregnancy. In these 6, the time interval between miscarriage and the time of admission extended from two weeks to one year; with the exception of the one patient who presented herself within two weeks, all were far advanced cases.

This one exception belonged in Stage I and this patient is now alive for eight years. There were 3 Stage III and 2 Stage IV cases, all treated in the usual manner and they all have died in a period of four days up to five years and three months.

One patient had palliation for a period of three or four years; subsequently developed recurrence and succumbed in five years and three months.

There were 5 patients who were admitted following normal deliveries and 2 patients who had had cesarean section previous to admission, one at one month and one at five months previously. In the 5 patients who had normal deliveries, from the time of delivery to admission the time extended from one and a half months up to eleven months. All of these patients gave a history of bleeding and discharge throughout the entire course of their pregnancy.

There were 5 State III and 2 Stage IV cases, and of these one Stage III case is alive and well for nine years; the rest of the patients died in periods of four months to one and a half years.

Now in addition to these there are 2 patients

who had had a delivery one year previous to admission and hysterectomy six months previous to admission. In other words, six months after the delivery; and a third patient who had a little bloody discharge two weeks before the expected date of delivery and in whom an early carcinoma was discovered. This patient had a cesarean section and total hysterectomy and following this a prophylactic course of high voltage roentgen rays and she is well for a period of eight years.

There were 2 other patients who, following miscarriage, were curetted and tissue taken from the cervix, and in both instances there was a questionable diagnosis of epithelioma of the cervix and both of these patients refused treatment on the basis that the diagnosis was questionable and they wanted children. They have been followed for two and three years, respectively, and there is no evidence of tumor.

A group such as this is too small to permit definite conclusions to be drawn, but of the patients with miscarriage there was one with a Stage I early lesion; that patient is well for eight years. Of the Stage II cases (those are the 2 patients who came to us pregnant with an associated carcinoma of the cervix), one patient is alive for six years and seven months.

Of the Stage III cases there were 8. One patient is alive for nine years, which would, on that small series, give about 12.5 per cent; and of the 4 Stage IV cases, there are none alive.

Of the 3 who had hysterectomy, there was only one early case and that patient is alive for eight years.

It has been our experience that the most important single factor in prognosis in carcinoma of the cervix, and it seems to apply here in carcinoma of the cervix associated with pregnancy, is the degree of anatomic involvement.

Dr. Herman C. Pitts, Providence, R. I. I want first to express our appreciation of this opportunity to give our results in the interstitial use of radium in cancer of the cervix.

In discussion I had in mind to say something of the difficulty in removing the long needles from the tissues after irradiation, and so I should like to answer Dr. Arneson's question of Dr. Waterman. We have found trouble at times in removing these needles,—in fact, so much trouble that we have had to resort to opening the abdomen in several cases to get the needles out finally, after hunting for them

through the pericervical tissue from below.

We have found now that by the use of Deknatel for threading the needles, that difficulty has been obviated. Deknatel has a tremendous tensile strength and by threading with this we haven't had any difficulty in several years. We tried at one time to use fine metal wire and that was the worst of all. That broke without any rhyme or reason.

When the end of the needle catches in the mucous membrane, if it has been pushed through under the mucous membrane, we have found that by coaxing with the finger, pushing it back and pulling it down, gently, we have been able to get it through the hole of entrance without making any incision in the mucous membrane, but that has been a difficulty that is quite apparent.

In respect to complications, there is one other I should like to speak of that Dr. Waterman touched on. That is the possibility of injury to the ureter. In one of my private cases the application of radium was followed by a stricture of the ureter that was perfectly apparent and which I relieved by opening the abdomen and transplanting the ureter into another place in the bladder wall. That worked perfectly well. She had no further difficulty.

I might say further that that patient finally died, in another city, of symptoms that suggested that she had had some injury to the intestinal wall followed by an obstruction and probable perforation of the intestine. The doctor who took care of her at that time wrote me the symptoms and I judged that something of that kind happened, although no operation was done. She had survived four years, when she died of this complication.

Before I came here I reviewed my own private cases from 1926 to 1934. There were 72 cases treated with radium needles, and this review upset a number of preconceived notions that I had regarding private cases. In the first place, I supposed that among the private cases I would find a larger percentage of Stage 1 cases. To my surprise, among the 72 cases I had just one Stage I case. There were 27 Stage II, 29 Stage III and 15 Stage IV cases.

The operability was quite high—38.8 per cent. It should have given me a better five year survival rate than 29.1 per cent.

I can only say that the one Stage I case I had survived the five years, which gave me 100 per cent on that. There were no survivals in the

Stage IV group. In that series there was no immediate mortality and aside from that one complication in the ureter there were no other complications that I noted.

There was one other thing of interest that I would like to speak of again that Dr. Waterman touched on. That is the surprising lack of complications from the entrance of these needles into the peritoneal cavity. We had occasion at one time to try a short series by implanting our needles and then opening the abdomen and tying off the circulation to the uterus. We tied off the ovarians and uterines on both sides, feeling that by that measure we might get a greater effect from our irradiation.

We did that on a short series and were rather appalled to find that in every case there would be a certain number of these needles sticking up into the peritoneal cavity but apparently they did no harm because there have been no untoward results reported in this series of ours.

DR. WILLIAM P. HEALY, New York City. I am very much interested in Dr. Taussig's paper. I think it is very nice indeed that his paper was presented here because he is making a splendid effort to improve his percentage of cures in the Stage II cases, and Dr. Pitts and Dr. Waterman were concerned about their Stage III cases, so we have had presented to us this morning two different approaches to the problem of the cure of carcinoma in the cervix but both in a sense touching upon, you might say, a surgical approach.

Dr. Taussig and all of us know that 30 to 50 per cent of cases of cancer of the cervix always have metastatic pelvic glands, and we all have realized that we are not getting in through the external portals enough radiation to clear up metastatic cancer in pelvic glands.

Therefore, I think that the approach that he is making is entirely justified, and I am delighted that it is being done by a man of Dr. Taussig's ability and repute, because if in time these results indicate that it is a procedure that should be followed, probably more of these operative procedures will be done. It isn't exactly the same thing, of course, as the dissection of the axilla in cancer of the breast, because there we take out the entire contents of the axilla, whereas Dr. Taussig restricts himself (I think) to lymphadenectomy alone.

I think it is impossible, by any paper work, to explain the difference in operability rates of

the cases in and about Providence and elsewhere.

Percentages that run from 36 per cent or almost 37 per cent to 38 per cent of operability are far above what we see around New York City and it was interesting that in that high total of all the cases presented by Dr. Waterman, not a single Stage IV case had survived; the Stage III cases are not as extensive, presumably, as the Stage III cases in the League of Nations classification, which must have a solid perimetrial fixation out to the bony pelvic wall on one side or the other in order to be Stage III.

But regardless of all our comment as to classification and grouping, we are delighted to be in a position to compliment Dr. Pitts and Dr. Waterman on their high percentage of cures which really does parallel their operability, because our own cures also largely parallel our operability.

When you get into the groups that have lymph gland involvement you are not going to cure them, in my opinion, with irradiation alone. You may add somewhat to the endresults with a lymphadenectomy or a Wertheim hysterectomy but not with irradiation.

Dr. Taussig (closing). I should like to add just a word to what Dr. Healy has just now said. That refers to the attempt to compare results from different institutions.

In the first place, the character of material coming to a cancer hospital is very different from that coming to a general hospital. We know that from experience in St. Louis. Many more advanced cases come to a cancer hospital. In the second place the method of classification of cases, of grouping, even when doctors say they are using the League of Nations classification, is not uniform in different institutions. My lymphadenectomy cases would be called Stage III according to the classification that has been usually employed by others. I call them Stage II because according to Heyman that is the proper terminology.

It seems to me the value of contributions in regard to the treatment of cancer arises from comparison of work in the same institution. If you change your treatment, under a fixed control, with the same method of grouping cases, and if you find this change of method causes improvement in your results, then you can say, if the cases are sufficient in number, that you have a definite improvement in tech-

nique; but to compare your results with other results in another institution means nothing at all.

Dr. Fricke (closing). I have nothing special to add except that these rare carcinomas of the cervical stump have interested us a great deal at the Clinic and there are always one or two patients who stand out. Two come to mind, one had been subjected to a supravaginal hysterectomy for fibroids two years previously and returned with a carcinoma, Grade 3, of the cervical stump which was classified as Stage III. This was treated and she returned for reexamination from time to time and the diseased condition had entirely cleared up.

In 1932 she came back with a totally different symptom and lesion. She then had an adenocarcinoma, Grade 2, of the rectum. This we treated with radium only. It has cleared up and she has remained well.

Another patient in another coincident group had been subjected to a chemical hysterectomy. This is the only case we included in which this type of operation had been performed. A year and a half later a carcinoma of the stump of the cervix developed. She was treated in 1930. The disease cleared up entirely and she was well, on frequent check-ups, for seven years or a little more than seven years. Then she returned with a massive recurrence or new growth. We treated her palliatively but she died a short time afterward.

Dr. Strauss (closing). I would like to add a word to what Dr. Wehr brought out concerning the postpartum cases. The cases of carcinoma of the cervix noted in the puerperium outnumber those discovered during pregnancy. They do not raise the same problems because the uterine cavity is empty and the life of the offspring does not come under consideration. Undoubtedly they should have been discovered during gestation.

There are some cases reported in which supracervical hysterectomy was done and this was followed by irradiation of the stump. I think that is not good procedure as Dr. Fricke has just brought out.

Dr. Pomeroy's case, which is in my paper, is very interesting from another viewpoint because it has not been reported before. It was treated in 1936 with an idea of quickly procuring a condition that would permit thorough irradiation. The patient was only four and a

half months pregnant and an abdominal hysterectomy was done and the fetus removed. I think that is better than doing a supracervical hysterectomy. Then she had thorough, heavy roentgen irradiation followed by heavy radium therapy, intrauterine, a little less than 2,500 mg-hr., and cervical treatment with radon seeds so that the treatment totaled almost 5,000 mg-hr. She is well to date.

Dr. Waterman (closing). I have been much interested in what Dr. Strauss has said about the treatment of cancer of the cervix complicated by pregnancy. We have in the last three or four years adopted a procedure somewhat similar to his. Where pregnancy has advanced four or five months and it does not seem advisable to wait for viability, we have been doing a hysterotomy high across the uterine fundus in order to keep the incision as far away from the cervix as possible. After removing the ovum the wound is closed and a ten day interval allowed for involution and healing to occur. It is then our practice to start treatment with deep roentgen therapy and radium according to our standard technique. This approach to the problem seems to us logical and we are going to see what can be done with it.

What Dr. Taussig says about classification of cancer of the cervix by different clinics is undoubtedly true. It is difficult to have agreement as to the different groups or stages even

if a definite classification can be accepted by all. A classification, however, is useful in a given clinic where the work is done by one or two men who check each other and have learned to agree quite consistently. Here comparison of results in different methods or from year to year may be fairly accurate. We have adopted the Schmitz classification and have used it through the years. If our results in a given class with a certain method show improvement over the results in the same class with a different method, we feel that something has been accomplished.

Dr. Healy has spoken of the high percentage of early cases, i.e. Stage 1 and Stage 11 in our series. It is true that we have a rather large number of favorable cases. It is also true that we do not have an excessive number of very advanced cases, i.e. Stage IV. I think this shows certainly that we are not increasing or improving the Stage III good results by placing some of the favorable borderline Stage II cases in this group; nor have we improved the results in the Stage III by placing some of the unfavorable borderline Stage III cases in the more advanced Stage IV group. It will be noted that our greatest improvement has been in the Stage III cases. This is the significant point that we wish to bring out as showing the value of interstitial irradiation of the parametrium with long platinum needles.



## TREATMENT OF POLYCYTHEMIA VERA BY ROENTGEN IRRADIATION OF THE ENTIRE BODY\*

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and

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SINCE the earliest description of polycythemia vera as a definite clinical entity, many different agents have been used in an effort to cure or control the disease. The most common are erythroblastic drugs, venesection, irradiation with radium or roentgen rays, oral administration of preparations of spleen, and gastric lavage. In this discussion we are principally concerned with the use of roentgen rays.

Undoubtedly because of the almost universal enlargement of the spleen in these cases, irradiation was first directed to this organ only, a practice which still persists in some localities. In 1916 Lüdin<sup>2,6</sup> first successfully irradiated the skeleton in addition to the spleen. His method consisted of using numerous portals, one or more at each sitting, and this plan with various minor modifications is probably the most widely used approach today. Langer,<sup>5</sup> in his irradiation directed toward the sympathetic nervous system, probably brought about the beneficial effects gained by the action of the roentgen rays on the vertebrae.

In 1927 Teschendorf<sup>9</sup> reported the use of teleroentgen therapy. As a therapeutic agent in the diseases for which it was introduced, namely, leukemia, lymphosarcoma, and Hodgkin's disease, it probably is no better than regional irradiation, and some observers consider it contraindicated.<sup>2</sup> Sgalitzer<sup>2,8</sup> began about this same time to treat polycythemia by Teschendorf's method, and he obtained good results even in cases that had been refractory to regional irradiation. By 1936 Sgalitzer had treated 44 patients, with good results in 42.

One patient died before proper conclu-

sions could be drawn, and one refused to complete the course of treatment. Sgalitzer felt, therefore, that he had benefited all the patients who had received adequate treatment. In one instance a patient remained well for three and a half years, then had a recurrence, was treated again, and was well two years after the second course of treatment. Sgalitzer fails, however, to give protocols or records of examinations of the patients' blood.

Teleroentgen therapy was first extensively applied in this country by Heublein,3 and like Teschendorf his cases consisted mainly of leukemia and Hodgkin's disease. Hunter,4 in 1935, published complete accounts of two patients with polycythemia vera who were treated by roentgen irradiation of the entire body. At that time the disease in both patients had been in remission for almost three years. One patient received only the initial series of treatment; the other received a second series at the end of one year, although the patient at the time was free from symptoms, and the blood picture was normal. At least one of Hunter's cases was reported in 1933 by Sanderson.7

Since 1936 we have treated 5 patients with polycythemia by the method of roent-gen irradiation of the entire body. We have been unable to follow the course of one patient, but we are reporting the other four in detail.

Our method of treatment conforms, in general, to that outlined by Sgalitzer, Sanderson, and Hunter. The patient is placed 2 to 2.5 meters from the anode of the therapy tube, either in a chair or on a stretcher.

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The patient faces the tube, with no lead protection of any kind. Thirty to 50 roentgens are given at a treatment, and treatments are administered every day or every second day. This dosage is measured at the patient's distance and also calculated from the intensity at 50 cm. by the inverse square law. In one instance I mm. aluminum only was used for filtration, but in all other instances I mm. aluminum and 0.5 mm. copper were used. The amount of filtration seemed to make no difference in the results. With 1 mm. aluminum and 0.5 mm. copper, 52 r were delivered in twenty minutes at a distance of 215 cm. (200 kv. (peak), valve tube, half-wave rectification, Villard condenser circuit, half-value layer of o.5 mm. copper: 1).

#### REPORT OF CASES

Case I (JHH 65656). K. W., a white woman, aged thirty-four, was admitted to hospital for

the first time in October, 1935, complaining of headache, dizzy spells, and redness and numbness of her extremities. The family and past histories were noncontributory. As early as 1933 her neighbors had commented on the redness of her hands and face. Her feet would become bluish when she was erect; she had occasional epistaxis; she would feel depressed and cry for no apparent reason; and the dizzy spells which occurred two or three times a week were not related to any particular activity. All her symptoms were becoming gradually worse at the time she was admitted.

Physical examination revealed weight loss, florid skin on the face and neck and to a less degree on the body, exceptionally red lips, much lymphoid tissue in the pharynx, and a "beefy" red tongue. The spleen was tender and extended 4 to 5 cm. below the costal margin. On admission the hemoglobin estimation was 144 per cent (21 gm.), the erythrocytes numbered 7,900,000, and the leukocytes 10,900 per cu. mm.

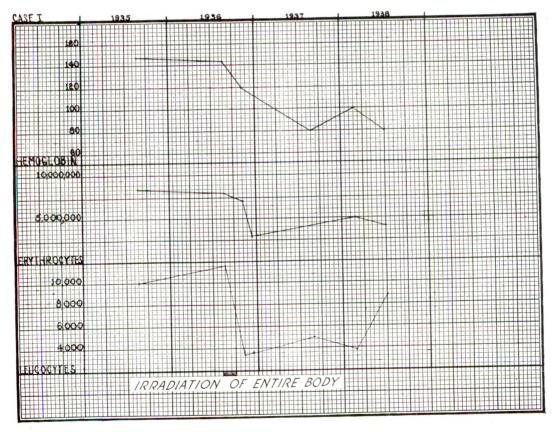


CHART I

Between October 22, and December 5, 1935, the patient received a total of 3.3 gm. phenylhydrazine, which she did not tolerate very well. Venesection was performed on December 12, and 500 cc. of blood was removed. She was discharged unimproved.

The patient returned to the hospital in July, 1936, with essentially the same symptoms and findings as the year before. During the interval there had been no relief from symptoms. The blood picture was as follows: hemoglobin estimation 130 per cent (21 gm.), erythrocyte count 7,500,000 and leukocyte count 19,000 per cu. mm.

Roentgen therapy by irradiation of the entire body was instituted on August 25, 1936, and completed on September 12, the patient receiving fourteen treatments of 52 r each. Chart I shows that the leukocyte count dropped steading to 3,200 per cu. mm., but the erythrocyte count and hemoglobin remained the same. No record of her blood is available again until November, 1936, at which time the erythrocyte count had dropped to 3,400,000 per cu. mm., and the leukocyte count had risen to 4,500 per cu. mm. The patient's progress since that time may be seen in the graph, and her physician states that she has been well since November, 1936.

CASE II (JHH 107653). We obtained our first record of this patient, S. S., a white woman, aged sixty-four, from a physician she consulted in 1926. Her blood picture at that time was as follows: estimation of hemoglobin 153 per cent, erythrocyte count 7,736,000, and leukocyte count 8,350 per cu. mm. During the spring, summer, and autumn of that year she received roentgen therapy over her spleen. The erythrocyte count remained essentially the same from May to December except for one recorded count of 3,000,000 in September. Shortly thereafter she consulted another physician who administered phenylhydrazine to her. Unfortunately, only a partial record of the blood picture is available until 1930.

In May, 1930, the patient entered the hospital for the first time. Her family history was noncontributory. She complained of dizzy spells and headache which she had experienced intermittently for seven years. She had been nervous for five years, and immediately previous to admission she had noticed palpitation and dyspnea on exertion. For one month before

admission she had no treatment with drugs, but she had been taking  $\frac{1}{2}$  pound of spleen a day.

Physical examination revealed a well developed, obese woman with a remarkable brick red color of face, neck, mucous membranes, and nail beds. The tonsils were enlarged. Blood pressure was 140 systolic and 90 diastolic. Examination of the blood resulted as follows: estimation of the hemoglobin 140 per cent (19.5 gm.), erythrocyte count 7,990,000, and leukocyte count 11,000 per cu. mm.

From May 11 to 19, 1930, she received orally 640 gm. of prepared spleen. On May 17 vene-section was performed, and 600 cc. of blood was removed. She was discharged unimproved. Between May, 1930, and March, 1931, she was bled twice by her family physician and received  $\frac{1}{2}$  pound of spleen daily for eight months.

She was readmitted to the hospital in March, 1931, with a blood picture as follows: estimation of hemoglobin 150 per cent, erythrocyte count 8,300,000, and leukocyte count 20,800 per cu. mm. Symptoms and physical findings were essentially the same as the year before except that arteriosclerosis seemed more noticeable, and the patient was more nervous and unstable emotionally. Blood pressure at that time was 175 systolic and 125 diastolic. During this visit she was given Fowler's solution, but its use was discontinued when she did not tolerate it well. Two venesections were performed, one of 700 cc. of blood and the other 1,000 cc. The patient was discharged in April without appreciable change in the blood picture.

When she was admitted to hospital in May, 1937, arteriosclerosis and mental confusion had increased. In addition, there was some pitting edema of the legs; the liver and spleen were each 4 cm. below the costal margins; the blood pressure was 260 systolic and 135 diastolic. Blood count was as follows: estimation of hemoglobin 135 per cent (19.5 gm.), erythrocyte count 8,500,000, and leukocyte count 26,500 per cu. mm.

The patient received roentgen therapy by irradiation of the entire body from May 18, 1937, through June 2, during which time ten treatments of 34 r each were given. She was discharged to the care of her local physician. Chart II shows subsequent reports on the blood picture. A report on July 7, 1938, stated that the patient, although deteriorating mentally, was maintaining a low normal erythrocyte count and hemoglobin and a normal leukocyte count.

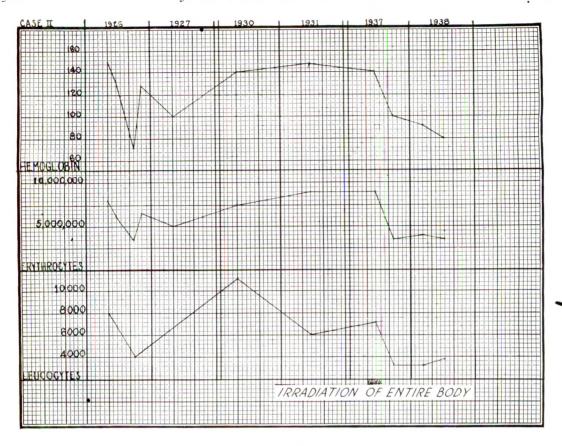


CHART II

Case III (JHH 116788). E. B., a white woman, aged fifty, was admitted to hospital in 1934 with a diagnosis of uterine myoma. The erythrocyte count was not recorded, but estimation of the hemoglobin was 82 per cent, and the leukocyte count was 9,200 per cu. mm. Hysterectomy was performed and after uneventful convalescence she was discharged without record of change in the blood picture.

From 1934 to 1937 the patient was seen in various dispensaries, but no examinations of the blood were reported. On September 1, 1937, the patient was admitted to hospital, suffering from dizzy spells, fainting spells, and "paralytic attacks." She dated her illness from the anesthetic taken in 1934. In 1935 she experienced nervous headaches, "tense" spells, choking sensations, and loss of appetite, sleep, and work. About this time she spent seven weeks in the psychiatric institute, where she complained of burning sensations as if her blood were on fire. These attacks continued until hospital admission in 1937.

Physical examination revealed a well developed woman whose face and extremities showed a distinct blush and whose tongue and mucous membranes were a deep red color. The spleen was 5 cm. and the liver 3 cm. below the costal margins. Peripheral arteriosclerosis was evident. Examination of the blood showed a hemoglobin of 138 per cent (20 gm.), an erythrocyte count of 5,460,000, a leukocyte count of 13,240 per cu. mm., and hematocrit of 58.5.

Roentgen therapy by irradiation of the entire body was instituted September 8, 1937, and continued through October 4, the patient receiving eleven treatments of 52 r each. On November 10, 1937, she reported that she felt much better. The liver and spleen had diminished in size. On December 12, two months after discharge from the hospital, the leukocyte count, which had dropped following treatment, was normal, and the hematocrit was reduced to 41.

Several furuncles developed about the face, but cleared up without difficulty. On February

5, 1938, the liver and spleen were just barely palpable, and the blood count remained normal. During April and May the patient suffered from recurrent furunculosis. The hematocrit was 48.5 on May 6, 1938, and the leukocyte count was 8,450. On June 20, 1938, she had no complaint, and the furuncles seemed to be healing.

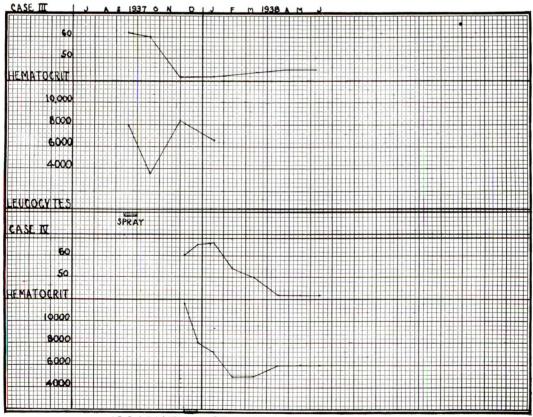
Case IV (JHH 127372). J. B., a white woman, aged fifty, was admitted to hospital December 8, 1937, complaining of weakness, pain in the left shoulder, headache, and some dizziness. The family history was noncontributory. In the patient's past history was a story of nervousness and emotional instability, for which she had been treated in the psychiatric institute. Beginning at the age of nineteen, she had been operated on many times, the last time in 1936. The blood count was found to be elevated at that time. For one year prior to her most recent admission to hospital she had noticed increasing weakness, fatigue, giddy spells,

and immediately prior to admission bluish spots on her extremities.

Physical examination revealed a fairly obese woman with dusky red skin. The lips and mucous membranes were very red, and the sclerae were injected. The liver was 3 cm. and the spleen 2 cm. below the costal margins. Several ecchymoses were present on the left thigh. Blood count showed a hemoglobin of 140 per cent (21 gm.), an erythrocyte count of 9,120,000, and a leukocyte count of 13,450 per cu. mm.; the hematocrit was 63.

Roentgen therapy by irradiating the entire body was started December 21, 1937, and completed January 5, 1938, the patient receiving ten treatments of 52 r each. She was discharged January 11, 1938, with a leukocyte count of 8,240 per cu. mm., although other elements of the blood picture remained the same as at the time of admission.

The patient was readmitted January 16 because unfavorable conditions at home prevented proper control. She noticed that she was



IRRADIATION OF ENTIRE BODY

Chart III

losing hair over the frontal region of her head. The hair subsequently became normal, and since there was no other loss of hair, the condition was assumed to be coincidental and not due to irradiation. The ecchymoses had disappeared, and the platelet count, which was low when therapy was completed, had returned to normal. The blood changes came about slowly, but eventually showed definite improvement (Chart III). The patient was seen last on June 23, 1938, at which time she was clinically in good condition, and the blood findings were normal.

Several points which call for discussion have arisen during the treatment and subsequent course of our patients. The leukocyte level was found to be the most accurate measure for determining the amount of treatment to give in any one case. Daily leukocyte counts should be made and when the number per cubic millimeter drops below 4,000, treatment should be stopped. If this rule is followed, an overdose can be avoided. The leukocyte count continues to drop for a short time after cessation of treatment, but then gradually returns to normal. Our charts prove that hemoglobin determinations and erythrocyte counts are unnecessary during therapy, because no change is evident in these elements until one to two months after the patient has been treated.

Objection has been raised about the latent period, that is the one to two months following therapy when erythrocytes, hemoglobin, and hematocrit remain high, while symptoms persist, and the use of phenylhydrazine and venesection during this period has been suggested. However, in some instances elevation of the leukocyte count follows use of phenylhydrazine. Anything which acts in such manner is dangerous when we remember that our index for therapy is the level of the leukocyte count. Venesection could be resorted to perhaps without danger, but the relief produced thereby is doubtful, and at best only temporary. We feel, therefore, that a short time of continuation of the symptoms is offset by the almost positive assurance of eventual relief.

Of the many methods used in treating patients with polycythemia, none seem to have produced so consistently the rather positive and prolonged relief from symptoms as that which has been gained from adequate roentgen therapy of the entire body in our cases and in those of Sgalitzer, Hunter, and Gilbert.2 It is true that one of our patients (Case II) is degenerating mentally, but it is also true that polycythemia was diagnosed in her case and that she was treated by other methods for eleven years before receiving roentgen therapy of the entire body. Possibly her present condition might have been averted had the polycythemia been arrested earlier. The other 3 patients, 2 of whom (Cases III and IV) possessed mild mental disturbances are certainly improved at the present time.

How long does remission last? The length of time will probably vary with the individual. In those cases reported here there has been no recurrence in twenty-three, fourteen, ten, and seven months respectively, and should signs or symptoms return to any one of them now, repetition of roentgen therapy of the entire body, from the standpoint of dosage, is not contraindicated.

This series of cases is too small for us to draw conclusions. We consider it important, however, to present our results and to corroborate the findings of the few other authors on this subject, namely, that roentgen therapy applied to the entire body at each seance is the most effective method to date for producing prolonged remission of polycythemia vera.

The authors wish to express their appreciation to Dr. Sarah M. Peyton of Crisfield, Maryland, for her very helpful coöperation in following two of the cases reported here.

#### REFERENCES

I. Connery, J. E. Treatment of polycythemia vera with phenylhydrazine hydrochloride and deep x-ray radiation. *Med. Clin. North America*, 1931, 14, 1569–1579.

2. GILBERT, R. Evolution of radiotherapy during the past ten years, in treatment of certain

4

- generalized affections. Radiology, 1938, 30, 191-
- Heublein, A. C. Preliminary report on continuous irradiation of the entire body. Radiology, 1932, 18, 1051-1062.
   Hunter, F. T. "Spray x-ray therapy" in poly-
- 4. Hunter, F. T. "Spray x-ray therapy" in polycythemia vera and in erythroblastic anemia. New England M. J., 1936, 214, 1123-1127.
- 5. Langer, H. Roentgen therapy in hyperplastic blood dyscrasias. Am. J. Roentgenol. & Rad. Therapy, 1935, 34, 214-233.
- 6. PACK, G. T., and CRAVER, L. F. Radiation

- therapy of polycythemia vera. Am. J. M. Sc., 1930, 180, 609-617.
- 7. Sanderson, S. S. Irradiation of entire body by the roentgen ray; preliminary report of twenty-two cases. Am. J. Roentgenol. & Rad. Therapy, 1036, 35, 670-680.
- THERAPY, 1936, 35, 670-680.

  8. SGALITZER, M. Röntgentotalbestrahlung bei Polycythaemie. Wien. klin. Wchnschr., 1935, 48, 675-677.
- TESCHENDORF, W. Ueber Bestrahlungen des ganzen menschlichen Körpers bei Blutkrankheiten. Strahlentherapie, 1927, 26, 720-728.



# OSTEOMYELITIS OF THE OCCIPITAL BONE COMPLICATING THE ROENTGEN TREATMENT OF A NASOPHARYNGEAL LYMPHOSARCOMA

By HENRY POTOZKY,\* M.D., and JACOB R. FREID, M.D. NEW YORK CITY

HE occurrence of neurological or I meningitic symptoms in the presence of a nasopharyngeal neoplasm is generally indicative of erosion of the base of the skull with invasion of intracranial contents by tumor or secondary infection. Such a phenomenon is particularly common in the evolution of the epitheliomas of the nasopharynx. As Furstenberg<sup>1</sup> has stated, these tumors have an irresistible tendency to grow upwards and invade bone, even when the primary tumor is very small. Thus, it is not infrequent for the lympho-epitheliomas to manifest themselves initially by symptoms referable to invasion of structures at the base of the brain (basilar syndrome). This syndrome has been studied particularly by the neurologists (Woltman,2 Needles3). The adenocarcinomas of the nasopharynx, which are usually slowgrowing tumors, will erode the base of the skull late in the course of the disease when they have attained considerable size.

In contrast to the carcinomas, it is extremely rare for the lymphosarcomas to erode the bony confines of the nasopharynx. Neurological complications of the nasopharyngeal lymphosarcomas presenting the picture of a basilar syndrome have been reported. Thus 4 such cases were present in Woltman's series and he collected at least 10 more from the literature. However, in none of these cases were postmortem examinations performed and the exact mode of invasion of the nervous system was not elucidated. It is possible that the structures at the base of the brain were involved, not by erosion of the tumor through bone but by spread of tumor along cranial nerves and extension into cranial foramina.

The invasive powers of these tumors, with respect to the surrounding bone, is in

inverse relationship to their radiosensitivity. Thus, the lymphosarcomas arising from the pharyngeal tonsils are very radiosensitive and may be totally destroyed in a high percentage of cases. Jutras4 reports that 89 per cent of the pharvngeal\* lymphosarcomas treated at the Radium Institute of Paris were permanently destroyed at their site of origin. The tendency to early and widespread dissemination was responsible for the eventual low five year \_ survival rate (25 per cent). Among New, Broders and Childrey's series of nasopharyngeal tumors, there were 15 lymphosarcomas. Four of these patients are alive after seventy-five months. In contrast to these results, the epitheliomas of the nasopharynx are very difficult to eradicate locally with radiation therapy and death is usually due to failure to control the primary site of disease.

In the case to be reported, a neurological and meningitic syndrome determined a fatal outcome during the course of treatment of a nasopharyngeal lymphosarcoma. One was forced to conclude that, despite adequate therapy, the tumor had continued to grow and had invaded the base of the skull, a difficult series of assumptions in face of the histological type of tumor under consideration. Postmortem examination revealed a totally different explanation for the chain of events leading to the patient's death.

#### CASE REPORT

S. S. (No. 28747), aged sixty, admitted to Montefiore Hospital November 11, 1937, with

<sup>\*</sup> This includes tumors arising from the nasopharynx, tonsil and base of the tongue.

<sup>†</sup> Our thanks are due to Dr. A. A. Schwartz who referred this patient for radiation therapy and with whose permission it is being reported.

<sup>\*</sup> Sigmund M. Lehman Fellow in Radiotherapy, Montefiore Hospital, New York.

a three months' history of increasing tinnitus, at first left sided and subsequently bilateral. During the four weeks preceding admission, tinnitus was replaced by deafness, which was more marked on the right. In addition, patient complained of dysphagia and severe headaches of a generalized character. Moderate nasal obstruction was present.

Positive findings on physical examination were limited to the nasopharynx, which was almost completely obliterated by a firm, edematous mass, most voluminous on the right and appearing to originate from the right pharyngeal wall. The mass was visible only on posterior rhinoscopy. It did not invade the nasal fossae. There was no cervical or remote adenopathy. Chest was negative.

Radiotherapy was started on November 1, 1937. Two large lateral fields (14×13 cm.), including the primary tumor and its lymphatic drainage, were treated. In the course of six weeks, patient received 2,300 r (measured in air) to each field. Factors were 200 kv., filter 1 mm. Cu and 4 mm. Al, target-skin distance 80 cm.; daily dose, from 150–200 r. The tumor

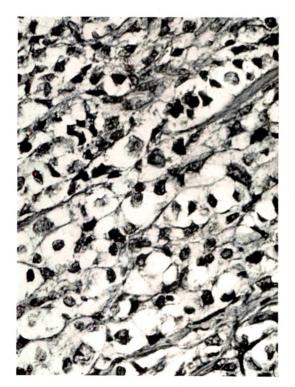


Fig. 1. Histology of tumor. Lymphosarcoma of reticulum cell type. Cells are stellate-shaped with cystoplasmic reticulum. ×480.

regressed satisfactorily under treatment. However, a necrotic ulceration developed in the tumor, probably starting at the site of biopsy (Fig. 1). Deafness became worse during therapy and headaches also became more marked. There was a severe epithelitis starting on the uvula on the fifth day of treatment and reaching a maximum on the seventeenth day. The soft palate, pillars and pharyngeal wall were also involved.

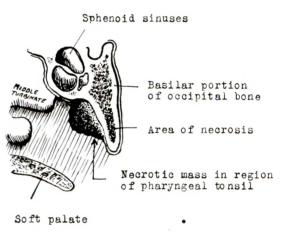


Fig. 2. Mid-sagittal section showing necrotic mass in region of pharyngeal tonsil as seen at autopsy.

Two days before the completion of treatment a paralysis of the left half of the tongue was noted. Headaches were becoming worse, especially in the right temporoparietal region. Four days later, the patient suddenly had a severe chill, became stuporous and cyanotic. The chill lasted for fifteen minutes and stupor for half an hour. Temperature rose to 105.5° F. The next day there were definite signs of a meningitis, bilateral Kernig's sign, stiff neck and Cheyne-Stokes respiration. Lumbar puncture revealed an initial pressure of 280 mm. of water, fluid was turbid, cell count 780 leukocytes with a predominance of lymphocytes. No organisms were present on smear or culture of the spinal fluid.

Signs improved in the course of the next day and spinal tap now showed normal pressure, only 260 cells, lymphocytes and no organisms. Unfortunately, the patient showed signs of a lobar pneumonia at this time and died December 13, 1937, from the pulmonary complication.

Postmortem Examination. Except for the lungs, which showed a confluent bronchopneu-

monia involving the entire left lower lobe, the positive findings were limited to the nasopharynx and adjoining structures. Overlying the region of the right pharyngeal tonsil, there was a necrotic hemorrhagic mass about 2 inches in diameter. A zone of necrosis of pharyngeal mucosa surrounded this area. The mass extended posteriorly to involve the right hypoglossal foramen. In a mid-sagittal section going through the sphenoid bone and basilar portion of the occipital bone, it was seen to be entirely extraperiosteal with no evidence of contiguous bone erosion or destruction. The bone marrow in the region of the occipital bone surrounding the foramen magnum was hemorrhagic and necrotic (Fig. 2). This process was seen to continue into the right basilar portion of the occipital bone and for a small area into the petrous portion of the temporal bone. The cortex of the bone was thinned out in areas but at no point was perforated. The dura, arachnoid and brain showed no gross abnormalities.

Microscopic. The soft tissue mass in the nasopharynx was necrotic fibrous tissue, infiltrated with inflammatory cells. There was no tumor present. The adjacent bone showed a diffuse osteomyelitis. There was no evidence of tumor invasion of bone.

#### DISCUSSION

The sequence of events in this case can be visualized as follows: Following irradiation, an already ulcerated and infected tumor underwent necrosis. The infection reached the adjacent bone marrow, probably through perforating lymphatics. This, added to damage inflicted by irradiation of the bone, resulted in an acute, rather fulminating osteomyelitis with blood stream invasion. The meningeal syndrome was probably a sympathetic meningitis due to the presence of a contiguous suppurative focus and not a bacterial meningitis. The tumor had been completely destroyed by irradiation. Death was directly due to pneumonia.

#### SUMMARY

A patient with a nasopharyngeal lymphosarcoma presented a meningitis syndrome during the course of roentgen therapy. At postmortem examination this was found to be due to an osteomyelitis of the basilar portion of the occipital bone and not to tumor extension through the base of the skull, as might have been expected.

#### REFERENCES

- Furstenberg, A. C. Malignant neoplasms of the nasopharynx. Surg., Gynec. & Obst., 1938, 66, 400-404.
- 2. WOLTMAN, H. W. Malignant tumors of the nasopharynx with involvement of the nervous system. *Arch. Neurol. & Psychiat.*, 1922, 8, 412.
- 3. NEEDLES, W. Malignant tumors of the nasopharynx. J. Nerv. & Ment. Dis., 1937, 86, 373-398.
- Jutras, A. Contribution à l'étude de l'influence des modalités radiothérapiques dans le traitement des sarcomes lymphoïdes du pharynx, etc. J. de radiol. et d'électrol., 1935, 19, 425-435.
- 5. New, G. B., Broders, A. C., and Childrey, J. H. Highly malignant tumors of the pharnyx and base of the tongue. Surg., Gynec. & Obst., 1932, 54, 164–174.



## **EXANTHEM COMPLICATING NEQPLASTIC DISEASE\***

#### ITS IDENTICAL OCCURRENCE IN FOUR CASES OF CARCINOMA

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SKIN reactions are expected locally as a response to roentgen therapy. Generalized skin reactions are unexpected and rare.

Arzt and Fuhs,1 after treating circumscribed areas of skin, occasionally noted a generalized, rapidly fading, scarlatiniform or fine papular rash associated with pyrexia. This was believed to be a toxic manifestation due to the absorption of cellular decomposition products caused by the roentgen rays. Enfield<sup>2</sup> described a rare roentgen toxic erythema which he thought was unquestionably due to the roentgen ray. He recorded 3 cases in which the rash was generalized, resembled scarlet fever and was accompanied by a febrile reaction lasting several days with temperature as high as 104° F. Pardo Castelló6 reported 4 cases of disseminated eruptions of the skin occurring after high voltage roentgen therapy. The patients had generalized symptoms consisting of malaise, nausea and vomiting, and slight elevation of temperature. Several days later 2 of the patients showed a morbilliform eruption; one showed disseminated areas of erythema, resembling erythema multiforme, and the other had large edematous papules on the trunk, neck and extremities, resembling the lesions of chickenpox in their initial stage. Subjective sensations were absent except for slight pruritus. The rash disappeared spontaneously except in the erythema multiforme cases where it lasted three weeks and gradually faded. Kautzky<sup>3</sup> stated that exposure to roentgen rays may provoke skin eruptions in patients with hyperthyroidism, psoriasis, and syphilis. He portrayed local reactions in 3 patients and a generalized urticarial reaction in one treated for

hyperthyroidism. He thought the reaction might be similar to skin sensitization resulting from barbiturate administration.

MacKee4 has seen skin reactions of the infectious eczematoid dermatitis type occurring beyond the local area being treated. Uhlmann<sup>11</sup> suggested that a generalized exanthem might develop after irradiation but doubted that such exanthems were caused by the roentgen ray per se. In twelve years of active practice he has never seen a true roentgen exanthem. In all cases coming under his observation, either an accidental concurrent septic exanthem or a suddenly developing erythroderma in psoriasis was demonstrated. He reported a case of a patient receiving radiation therapy to the pelvis for a uterine cancer who developed a scarlatiniform rash from head to feet, with swelling of the evelids and ankle edema. The patient's condition was poor. A diagnosis of a generalized roentgen exanthem had been made. However, the patient was found to be taking at least eight tablets daily of a barbiturate preparation (optalidon plus sandopta). Four days after this was discontinued the skin reaction regressed. He admitted the possibility of a true roentgen exanthem but believed a summation effect between the barbiturates and the therapy a more plausible cause.

Trostler<sup>9</sup> felt that barbiturates may sensitize the skin to radiation therapy. He stated that many commonly used sedatives such as sulphanol, luminal, and other barbituric acid derivatives produce porphyrinemia and porphyrinuria with resultant sensitization to light and radiation. He saw 3 cases in which severe local reactions, apparently roentgen erythema, occurred. He concluded that the cutaneous response was

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due to the concomitant use of barbiturates. In another communication<sup>10</sup> he referred to Uhlmann's case mentioned above, and pointed out that the barbiturates taken by the patient caused a porphyrinemia and porphyrinuria. He explained the rash on this basis.

However, the porphyrins produce a definite syndrome which has not been demonstrated in Uhlmann's or Trostler's cases. Mason, Courville and Ziskind<sup>5</sup> stated that in every case of hematoporphyria acuta toxica reported up to 1933, the symptoms followed long continued abuse of sulphanol, trianol, and possibly veronal. As a rule, the drug had been taken in daily doses of at least a gram for fully a year before symptoms appeared. Manifestations of the disease have never been reported in acute intoxications with any of these drugs. Kaplan<sup>12</sup> has never observed any rashes similar to those reported by Uhlmann and by Trostler although he has frequently given barbiturates to patients receiving radiation therapy. Richards and Peters<sup>8</sup> and Popp and Binger<sup>7</sup> gave barbiturates in order to diminish radiation sickness. They observed no rashes although other evidences of idiosyncrasy were evident in one patient.

It is difficult to determine from this review of the literature whether a uniform clinical syndrome with a common etiology has been described. Our own experience with 4 essentially similar cases of exanthem occurring after radiation therapy would seem to indicate that we are dealing with a hitherto undescribed entity, having an identical etiology. We present them in order to stimulate further reports and efforts to elucidate the precise causative factors.

#### REPORT OF CASES

Case I. A white male, aged sixty, was admitted to the Brooklyn Cancer Institute of the Kings County Hospital on November II, 1937, with a proved diagnosis of squamous cell carcinoma of the tongue and submaxillary metastases. His family and past history was irrelevant except for asthma of five years' duration. A 3 cm. indurated lesion, surrounded

by a few leukoplakic spots, was present on the left side of the tongue. A small hard gland was felt in the left submaxillary region. Physical examination was otherwise negative. The Kline test was negative. Urine examination was normal. Blood count: hemoglobin, 70 per cent; red blood cells, 4.78 million; white blood cells, 5,600, with 76 per cent polymorphonuclears, 24 per cent lymphocytes and no eosinophiles.

On November 18, 1937, ten 2 mg. radium needles were inserted and 2,000 mg-hr. of radium given. On November 26, radiation therapy was started via one anterior, one lateral and one posterior 6×8 cm. portal which included jaw and neck. Two hundred roentgens were given daily through each portal with 200 kv., 20 ma., 50 cm. skin target distance and 2 mm. Cu plus I mm. Al filter as factors. On December 8, when he had received 1,600 r anteriorly and posteriorly and 1,800 r laterally, • the skin erythema was so severe as to preclude further therapy through these portals. On December 9, intraoral cone therapy was started and patient had received 1,400 r by December 16 when treatment was discontinued.

On December 20, 1937, he complained of stuffed nose, pain in eyes, and pain and burning in mouth. This is taken as the first day of his current illness. On the third day he complained of pain in the throat. On the sixth day his temperature rose to 101.2° and two days later to 102.6° F. He was acutely ill. At this time a generalized erythematopapular rash was noted for the first time. It was present on the neck, trunk, scrotum and extremities, including palms and soles. There was a tender erythema on the face extending beyond the portals exposed to roentgen radiation. The eyelids, bridge of nose and circumoral region were involved. There was a bilateral conjunctivitis. The lesions resembled erysipelas. The mucous membranes of the mouth, throat and nose were extensively involved in a membranous ulcerative process which extended beyond the area treated and was of greater severity than could be expected from a radiation response. Indeed it was so severe as to be thought diphtheritic. His temperature fluctuated irregularly between 99 and 104° F. The face lesions became vesicular, bullous, hemorrhagic and, six days later, crusted. The body lesions became more intense for about three days, remained stationary for a short time and then began slowly to recede. However, the patient continued to be acutely ill. Blood culture on the twelfth day was negative. Throat cultures taken on the same day showed no diphtheria or Vincent's organisms. Staphylococcus albus and aureus were present. On the seventeenth day, the throat revealed the same organisms. On the nineteenth day the throat culture showed Streptococcus anhaemolyticus and Staphylococcus albus. A culture taken from beneath a crusted lesion on the neck showed Staphylococcus albus and aureus and diphtheroids. Cultures taken from intradermal region of skin lesions were negative. Blood count taken on the eighteenth day showed 3.6 million red blood cells, 11,800 white blood cells, with 42 per cent polymorphonuclears, 2 per cent basophiles, 43 per cent eosinophiles and 13 per cent lymphocytes. Chest roentgenogram taken the same day was negative.

On the twenty-second day of illness, two weeks after their appearance, the face lesions had crusted and fallen off and the skin lesions were almost invisible. Because the patient had been receiving at least a grain and a half of phenobarbital almost daily since admission, this was considered as a possible etiological factor. However, the rash faded although the barbiturates had been continued. The clinical course also spoke against barbiturate poisoning. The patient continued to be critically ill and on the twenty-first day his temperature began to spike, rising to 105° F., on four days. His skin condition had almost entirely disappeared and it was felt that a complication had developed. Blood cultures taken, anaerobically and aerobically, on the twenty-second, twentyfifth, twenty-sixth and thirty-first days were all negative. Widal test done on the twentythird day was likewise negative. Urine, negative on the twenty-first day, had occasional white blood cells on the twenty-second day. The blood count on the twenty-fourth day showed hemoglobin, 51 per cent; red blood cells, 3.04 million; white blood cells, 12,650, with 63 per cent polymorphonuclears, I per cent basophiles, 18 per cent eosinophiles, 2 per cent monocytes and 16 per cent lymphocytes. Repeat blood count on the thirtieth day disclosed hemoglobin, 53 per cent; red blood cells, 3.15 million; white blood cells, 9,350, with 85 per cent polymorphonuclears, 3 per cent staff cells, I per cent eosinophiles, I per cent monocytes and 10 per cent lymphocytes. On the thirtysecond day his blood chemistry was urea nitrogen 12.72 mg., creatinine 1.5 mg. and sugar 111 mg. per 100 cc. of blood. During the time his temperature was spiking, he developed a cough and became irrational. It was felt that he had bronchopneumonia. In spite of all supportive efforts, including a blood transfusion on the twenty-eighth day, the patient died thirty-five days after onset of illness. Autopsy was not obtained.

Case II. M. C., a white female, aged forty-eight, entered the hospital on December 7, 1937, with a proved diagnosis of transitional cell carcinoma of the pharynx with bilateral cervical gland and possible right petrous bone metastases. Her family and past history was irrelevant. Between August, 1935, and September, 1937, she had received elsewhere a total of 15,400 r with varying factors to various portals about the neck and pharynx, especially on the right. Included, were 1,000 r given intraorally during June, 1937.

Her skin was deeply pigmented over the right cervical region. A 2 cm., hard, fixed gland was found under indurated skin in the region of the lower portion of the sternomastoid. Firm, deep cervical glands were palpable on the left side. The pharynx showed no gross neoplastic masses but contained a large amount of mucus. She had a bilateral horizontal nystagmus and nerve deafness of the right ear. Physical examination was otherwise negative. Her blood count before admission was hemoglobin, 86 per cent; red blood cells, 4.15 million; white blood cells, 5,750, with 68 per cent polymorphonuclears, 32 per cent lymphocytes and no eosinophiles. The Kline test was doubtfully positive. Urine examination on admission showed occasional red blood cells but next day was negative. On December 11, 1937, the right petrous bone was exposed but no metastases were found. She recovered uneventfully except for a herpes labialis.

On January 1, 1938, she complained of nasal congestion, bloody, mucoid nasal discharge and postnasal drip for which ephedrine drops were prescribed. This is called the onset and first day of illness. Between January 3 and 8 she received therapy to her left cervical metastases, through one anterolateral and one posterior portal. Factors were: 200 r daily through 6×8 cm. portal; 200 kv., 20 ma., 50 cm. skin target distance, 2 mm. Cu, 1 mm. Al filter. During this time, 1,200 r had been given through each

portal. The blood count taken on January 4, showed hemoglobin, 60 per cent; red blood cells, 4.05 million; white blood cells, 3,600, with 73 per cent polymorphonuclears, 4 per cent monocytes, and 23 per cent lymphocytes. She complained of headache and nausea. On the sixth day she had a sore throat. On the eighth day she was acutely ill and a patchy, macular dermatitis was noticed on cheeks, nose and lips, well beyond the treated area. The mucous membrane of the mouth, nose and throat resembled a severe Vincent's infection. Next day her temperature rose to 102.8° F. On the eleventh day the face rash had become maculopapular but was limited to face and neck. The left ear was swollen and glazed and resembled erysipelas. The mucous membranes showed oval lesions I cm. in diameter, with a gray membranous necrotic surface surrounded by a small area of erythema. No Vincent's organisms were present. Neosalvarsan injections did not improve the condition. Throat cultures revealed Staphylococcus albus and Streptococcus haemolyticus. Urine examination was negative. Blood count showed hemoglobin, 62 per cent; red blood cells, 3.54 million; white blood cells, 5,000, with 64 per cent polymorphonuclears, 1 per cent staff cells, 2 per cent monocytes, 7 per cent eosinophiles, and 26 per cent lymphocytes. Because the patient had been given between  $1\frac{1}{2}$  and 3 grains of phenobarbital almost daily since admission this drug was held responsible and was discontinued. Apparently, however, this did not vary the course of the disease. Her temperature continued to range between 100 and 102° F. By the thirteenth day the face lesion had become confluent. The leukocyte count was 6,500, with 78 per cent polymorphonuclears, 2 per cent monocytes, 5 per cent eosinophiles and 15 per cent lymphocytes. The next day her temperature rose to 103° F. Millet to pea-sized, discrete, sparsely distributed, dark red, maculopapular lesions were noted on the arms, dorsum of hands, abdomen, back and legs. Blood culture was negative aerobically and anerobically. Throat cultures revealed Staphylococcus albus and Streptococcus non-haemolyticus. Urine showed an occasional leukocyte and red blood cell. The confluent lesions on the face became vesicular on the sixteenth day. Following this they became bullous, hemorrhagic and began to crust two days later. Biopsy of a lesion on the forearm revealed a surface lining epithelium which was

histologically normal. The underlying corium presented some edema and a scant perivascular infiltrate of lymphocytes and occasional polymorphonuclears. The lesion was felt to be nonspecific. The leukocytes on that day were 7,950 with 77 per cent polymorphonuclears, 2 per cent monocytes, 2 per cent eosinophiles and 19 per cent lymphocytes. The temperature had begun to recede by lysis. When it rose again from 98° to 101° F. on the nineteenth day, the blood culture was repeated and found negative aerobically and anaerobically. The urine showed an occasional leukocyte and red blood cell. The Kline test was repeated and found negative.

The temperature fell steadily thereafter and by the twenty-third day had been between 98 and 99° F. for two days. The crusts had dried and fallen off the face, the body lesions faded, and the mouth lesions improved. She was discharged on the thirty-second day.

CASE III. A. F., white male, aged seventyeight, with a proved diagnosis of squamous cell carcinoma of the cheek and cervical metastases, was admitted to the Brooklyn Cancer Institute of the Kings County Hospital on February 9, 1938. His family history was irrelevant. His past history included erysipelas of the face thirty-five years prior to admission. His left cheek was indurated externally and disclosed an extensive neoplastic growth internally which covered the entire buccal area. In the left submaxillary region was a marble-sized hard, fixed gland. Physical examination was otherwise negative. Blood count on February 11, 1938, was hemoglobin, 75 per cent; red blood cells, 3.9 million; white blood cells, 9,800, with 70 per cent polymorphonuclears, 2 per cent monocytes, no eosinophiles and 28 per cent lymphocytes. Urine examination was negative. Wassermann and Kline tests were negative.

Between February 10 and March 11, 1938, he received 2,000 r to each of three portals crossfiring the left cheek, as well as one intraoral portal of 2,000 r. The factors previously employed were used here. On March 1, 1938, radiation reaction was first noticed on the mucous membrane and skin. On March 9, the onset day of his present illness, he first complained of soreness, pain in the mouth and sneezing. On March 13 an extensive, generalized, membranous, ulcerative buccal eruption

resembling the two previous cases was seen. His urine showed a I plus albumin and an occasional leukocyte and red blood cell. His temperature was 101.6° F. On March 18, the tenth day of his illness, it was noted that the patient developed an erysipeloid eruption, extending considerably beyond the area exposed to radiation therapy. Both sides of his face, especially the left, were involved. He had a bilateral conjunctivitis. His temperature was 101.8° F., and multiple, discrete, small macules, dull red in color, appeared on both forearms and hands and a few on the chest, abdomen and legs. Until the eleventh day of illness he had received, almost daily, small amounts of phenobarbital. This was discontinued but the condition, nevertheless, progressed. The rash on the face progressed similarly to Cases I and II, becoming confluent, vesicular, bullous, hemorrhagic and crusted by the seventeenth day of illness (Figs. 1, 2, and 3). The macules on the arms, chest, back and legs increased in intensity for several days and then gradually receded. There were no Vincent's organisms isolated from the mouth. On the thirteenth

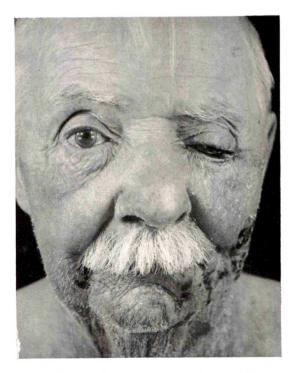


Fig. 1. Case III. Squamous cell carcinoma of buccal aspect of cheek, sixteenth day of exanthem. Note pronounced reaction about eyelids which were not subjected to radiation therapy.

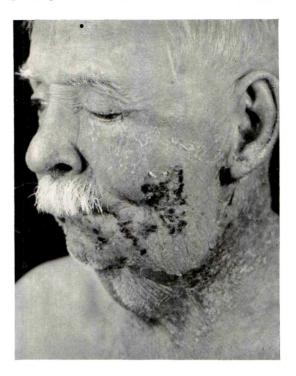


Fig. 2. Case III. Note confluent, vesicular, hemorrhagic, crusted lesion of cheek and glazed appearance of ear.

day, Wassermann and Kline tests were repeated and found negative. Blood chemistry was normal. His urine on the following day contained 2 plus albumin with an occasional leukocyte and red blood cell.

On the sixteenth day of illness the aerobic and anaerobic blood cultures were negative. Staphylococcus aureus and diphtheroid bacteria were isolated from the left side of his mouth and Staphylococcus albus and diphtheroids from the right side. Cultures of a cutaneous lesion on the chest yielded Staphylococcus albus and aureus and Streptococcus nonhaemolyticus. Widal examination was negative on the next day. Biopsy of a maculopapule on the right arm was performed and histopathological study showed an intact lining epithelium with a moderately edematous underlying corium and a perivascular lymphocytic infiltration. There was a moderate increase in fixed tissue cells. The diagnosis was nonspecific dermatitis. By the twentieth day of illness the face lesions had crusted and the body lesions had almost completely vanished. The blood count was hemoglobin, 72 per cent; red blood cells, 3.64 million; white blood cells, 10,400,

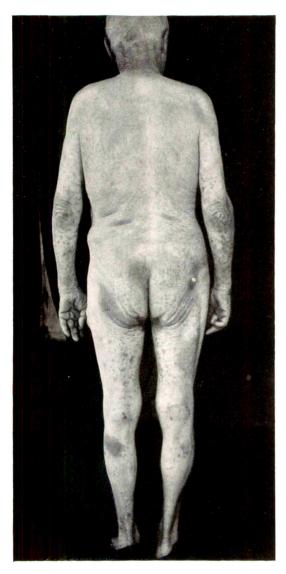


Fig. 3. Case III. The generalized character of maculopapular exanthem is well demonstrated. In areas the lesions have coalesced.

with 72 per cent polymorphonuclears, I per cent monocytes, 4 per cent eosinophiles, and 23 per cent lymphocytes. Several lesions on the extremities were severely excoriated due to itching. These became secondarily infected. His temperature fell by lysis concurrently with the fading of his skin lesions and he appeared to be recovering from his initial acute exanthem. However, it so completely exhausted him that he developed a bronchopneumonia to which he succumbed on the twenty-fourth day.

Necropsy by Dr. H. Bolker revealed the following pertinent findings:

Gross: The skin of the left side of the face, ear and neck is discolored purple and covered by fine flaky scales. One area 2×1 cm. on the left cheek is covered by a somewhat thicker brownish scale. The scaling appearance is rather prominent in the folds of the left neck. The ocular conjunctiva on the left is covered by a milky mucoid material. The conjunctival vessels are congested. The cornea shows no changes. The lips, mouth, tongue and pharvnx are covered with a dirty mucoid material. In the left buccal mucous membrane is an irregular indurated neoplastic area. On the outer aspect of the left arm 6 cm. above the elbow is an ulcer 2 cm. in diameter which extends through the skin, reaching the underlying muscle; its base is covered by a greenish, necrotic material. There is a reddish area I cm. in diameter covered by a fresh crust on the dorsum of the left hand. Several similar areas • are found on the right hand, wrist and forearm. There is a suggestion of a macular rash barely visible on the anterior chest wall. Recent excoriations are present on the left chin, one in its mid-portion 3 inches in length and one in its lower third  $\frac{1}{2}$  inch in length. A diffuse bronchopneumonic process is present in both lungs. Remainder of gross necropsy findings are irrelevant.

Microscopic examination:

Mouth lesion: A portion of the section is lined by histologically normal stratified squamous epithelium, infiltrated with occasional polymorphonuclear leukocytes. The lining is absent in one area, the base of which is a necrotic, purulent layer. The underlying tissue contains numerous, thin-walled, dilated and congested capillaries, a heavy infiltrate of plasma cells, lymphocytes and polymorphonuclear cells and sheets of invading neoplastic cells of the prickle cell type undergoing degeneration. Numerous small areas of keratinization are definable. There is invasion into the muscular layer, the muscle bundles undergoing degeneration. Large numbers of foreign body giant cells are present in the tumor areas.

Oral mucosa: Sections through the adjacent oral mucosa are lined by epithelium, showing degenerative changes. The underlying tissue is granulation in type.

Skin lesions: All the lesions present a similar picture, more or less marked in different areas. The surface epithelium is undergoing degeneration to varying degree and is covered by a

parakeratotic layer, heavily infiltrated with polymorphonuclear leukocytes. The underlying stroma is edematous, contains numerous, thinwalled, congested capillaries and a leukocytic infiltrate, chiefly perivascular, of the polymorphonuclear and plasma cell varieties. The inflammatory picture is particularly marked in the sections from the left arm, where the deeper layers of the corium and the subcutaneous fatty tissue are the seat of large collections of polymorphonuclear leukocytes, forming localized abscesses. The inflammatory reaction extends into the fatty tissue over wide areas. Similar smaller abscesses are found in the lesions of the left hand. Here the entire epidermis has been replaced by a necrotic layer. Giemsa and Gram stains show the presence of numerous Gram-positive cocci in pairs of short chains in the corium of many of the sections (Figs. 4 and 5).

Lungs: There is moderate subpleural anthracosis. Groups of alveolar spaces have their lumina crowded with polymorphonuclear leukocytes. The corresponding alveolar walls are widened due to capillary congestion. Many of the remaining alveolar spaces are emphysematous. The bronchial lining epithelium is well preserved, the lumina occasionally containing polymorphonuclears.

Case IV. M.S., white female, aged seventy-five, entered the hospital on March 16, 1938, with a proved diagnosis of squamous cell carcinoma of the hard palate. Her family and past history was irrelevant. On the right anterior



Fig. 4. Case III. Photomicrograph of section of skin of neck from early lesion showing acute inflammation, edema, vascular congestion, diffuse polymorphonuclear leukocytic infiltrate and parakeratotic layer (×80).

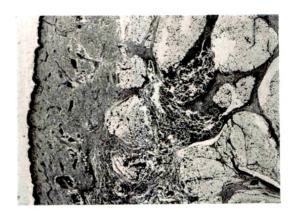


Fig. 5. Case III. Photomicrograph of section of skin of left arm from a more advanced lesion showing subcutaneous abscess and marked dilatation and congestion of blood vessels in the corium (×12).

portion of her hard palate was an ulcerative, hard, neoplastic area with raised edges and a perforation into the maxillary sinus in its midportion. Two firm glands, one marble-sized and the other walnut-sized, were present in the right submaxillary region; a marble-sized one on the left. Physical examination was otherwise negative. Kline and urine examinations were negative.

On March 18, 1938, roentgen therapy was begun to four portals: a right and left lateral cheek portal, one anterior and one intraoral portal. Factors similar to the previous cases were used. Two hundred roentgens were given daily to each portal rotating right and left. On March 29, 1938, when she had received 800 r to each of the four portals, a pseudomembranous brownish slough of the mucous membranes of the palate and cheeks was noted. Although this was attributed to irradiation, it may well be the onset of the illness under discussion. Her blood count that day was hemoglobin, 92 per cent; red blood cells, 5.2 million; white blood cells, 9,000, with 57 per cent polymorphonuclears, I per cent staff cells, 2 per cent monocytes, 12 per cent eosinophiles, and 28 per cent lymphocytes. Her temperature was normal.

On the third day, it rose to 100.2° F. Vincent's organisms were absent from the mouth smears. *Staphylococcus aureus* was present. By the seventh day, her temperature had fallen to normal. Therapy was continued. On the thirteenth day, pea-sized, red, macular areas were noted on the left cheek. The temperature rose to 100.2° F. By then she had received 1,600 r to

all the portals except the left cheek, which received 1,400 r. The next day both cheeks were involved and her temperature rose to 100.8° F. The mucous membranes of the cheeks and lips had small, discrete, pea-sized, oval or round, irregularly-edged, whitish areas surrounded by a deep erythematous base. They appeared at sites apparently beyond the areas exposed to the roentgen ray. Lesions on the face resembled cases seen previously but the severity and generalization were absent. The next day her temperature fell to 99° F. The nurse reported a "prickly heat" type of rash on the back but this faded quickly and was not seen on the eighteenth day when her temperature was 100.2° F. Her temperature fell quickly to normal.

The lesions on the face extended beyond the areas treated but were extremely mild in severity. By the twentieth day they had become confluent and scaling. Her temperature was normal until the twenty-fourth day. Blood count then was hemoglobin, 101 per cent; red blood cells, 4.2 million; white blood cells, 6,000, with 69 per cent polymorphonuclears, I per cent monocytes, I per cent basophiles, 2 per cent eosinophiles, and 27 per cent lymphocytes. Following the development of a cervical adenitis and rise in temperature to 101° F. for two days, she made an uneventful recovery. By the thirtieth day her facial lesions had entirely faded. She still had small areas in the mouth resembling Vincent's patches. During this entire period she was deemed well enough to continue with her radiation therapy. She received 2,200 r to the intraoral portal, 2,000 r to each of three face portals, 2,000 r to two right neck portals and 2,000 r to two left neck portals. In all she received 16,200 r to her skin via various portals. During her entire stay she received 11 grains of luminal daily for restlessness and insomnia. She left the hospital improved on July 9, 1938.

#### DISCUSSION

Of exceptional interest is the fact that the course, pathology, and laboratory data of all 4 cases were so similar as to suggest a distinct clinical entity. All the cases received roentgen therapy in varying amounts about the neck or buccal cavity for carcinoma of tongue, nasopharynx, cheek or hard palate. Coincident with the irradia-

tion or shortly thereafter, all had complaints such as soreness, pain in mouth and sneezing with mucoid bloody discharge. The severity and extent of the reaction could not be explained as a response to roentgen therapy alone, the mucous membranes being involved in areas apparently beyond those exposed to radiation. The face lesions likewise appeared far beyond the area exposed to radiation therapy and could not therefore be ascribed directly to the roentgen ray. In each instance, approximately the same time after the initial complaints, the face lesions appeared; in the first two cases on the eighth day of illness; in the third case, on the tenth day; and in the fourth on the thirteenth day. In the last case as a result of our previous experiences the initial mouth lesions were discovered earlier before subjective symptoms supervened. This may explain the apparently delayed appearance of the face lesions. In all, they first appeared as discrete macules, which became in turn confluent, vesicular, bullous, hemorrhagic, scaled, crusted and dried.

The number of days from appearance to crusting was approximately eight, ten, seven and seven days, respectively. The rashes which appeared on the body were similar. They were first discovered on the eighth, fourteenth, tenth and seventeenth day of illness, respectively. An adequate explanation for the relatively delayed appearance in Case IV has been advanced. All were of a discrete, erythematous, maculopapular type and generally distributed. The skin lesions in the fourth case were evanescent. In the first 3 cases the exanthem lasted approximately nineteen, eleven, and fourteen days, respectively. Coincident with the face and skin lesions the temperature attained high levels and receded by lysis as the rashes faded. Secondary rises in temperature indicated a complication. All the patients were severely toxic. An eosinophilia was common to all. None showed a leukocytosis unless a complication arose. Urine examinations indicated renal disturbance in the first 3 cases.

Blood cultures were invariably negative. Skin and mouth cultures revealed no extraordinary organisms. Intradermal skin cultures of the body lesions were negative in the first case. Biopsy of one of the generalized skin lesions in Cases II and III showed, in each instance, an edematous corium with a perivascular infiltrate of lymphocytes and polymorphonuclear leukocytes. The skin findings at necropsy in the third case were those of secondary infection. Clinically and pathologically the cases resembled each other to a remarkable degree.

An attempt to identify precisely the causative factor or factors would be more or less speculative. Certain clinical entities with which the condition under discussion may be confused can be excluded. Thus, barbiturates were held responsible in some cases previously reported, and suspected to some extent in our own patients. In the previously reported cases the causal relationship is not proved beyond a doubt. Of interest in this connection is the fact that in our Case I the rash receded in spite of the continuance of barbiturates. In Case II the rash progressed despite the discontinuance of the drug. In Case IV, which presented but a mild and evanescent eruption, barbiturates were given over a prolonged period. The exanthems were in all respects similar regardless of barbiturate intake. We have given barbiturates to many patients receiving roentgen therapy, and for long periods of time, without noting a similar reaction. We feel justified in dismissing barbiturate intoxication as a probable primary etiologic factor.

Eczematoid dermatitis, as described by Fordyce, was considered. We have seen several such cases which had their origin in proximity to irradiated areas which were superficially infected or suppurating. These cases bore no resemblance to those under discussion.

Erysipelas had to be ruled out since the face lesions resembled it at one time or another, particularly in the early stages. Case III gave a history of erysipelas thirty-five years previously. The mode of onset, course,

generalization of the rash and absence of leukocytosis all spoke against erysipelas. Finally, there was a total lack of response to sulfanilamide therapy. Vincent's organisms were not found in any case. Neoarsphenamine had no effect on the lesions.

The organisms isolated from the mouth were not remarkable, and there is little likelihood that they were the causative factors. One would expect them in any excoriated lesion of the mucous membranes. Diphtheria organisms were never found. The therapy machines used to irradiate these patients were suspected as a possible source of infection. The intraoral cone, the rubber cots used to cover it, and the surface of other cones used were cultured and revealed nothing extraordinary. Other patients treated with the same apparatus during the same period were unaffected.

Undoubtedly the local lesion was due, in part, to the extensive roentgen-ray exposure. In no way, however, could we ascribe the entire picture to the roentgen therapy. Thus, Case IV received 16,400 r about the face and neck with the mildest resultant reaction of the 4 cases reported. Other cases treated similarly showed no generalized response. In every case the rash spread well beyond the area exposed. Finally, the picture did not resemble that of any of the known exanthems.

A generalized skin and systemic reaction was noted. A solution of continuity of skin and mucous membrane was occasioned by tumor formation and aggravated by roentgen therapy. Following irradiation there is a great breakdown of tumor tissue, contiguous normal skin, and mucous membrane. Combined with this is a local vascular disruption. There is thus provided not only an ideal nidus for toxic and infectious agents, but an excellent portal of absorption as well. As a contributory factor the usually weakened condition of the cancer patient undergoing therapy cannot be disregarded.

From the facts available at present, it is impossible to identify precisely the factor or factors responsible for the disorder.

However, several explanations appear plausible. The products of cellular decomposition absorbed into the blood stream may well have caused an allergic or toxic reaction. Indeed such a cytotoxic absorption could hardly be avoided. The eosinophilia, observed in all our cases, suggests such a protein absorption. Similar reactions might be expected wherever radiation reactions were taking place. Skin lesions reported following irradiation of other areas may be rationalized on this basis. If this were actually the case, the gross picture of the toxic response might be the same, but one would expect wide differences in its severity and course depending upon such variables as the amount of cytotoxic substance absorbed. On the other hand, while some cytotoxic absorption must invariably take place following tissue breakdown, generalized reactions, as herein described, are extremely rare. Similarly our first 3 cases were so alike in onset, severity, and day by day course that one must suspect some other mechanism at work. The type of response speaks for a common, constant, causative factor possibly of infectious character. The lowered resistance of the host. the excellent medium for bacterial growth in the broken down tissue, the convenient portal of entry, tend to make this probable. The usual bacteriologic tests revealed primarily the customary non-pathogenic variety of organisms. The rarity of the condition and absence of leukocytosis speak for a bizarre infectious agent, possibly a filterable virus.

We have by no means exhausted all the possibilities but have made a few suggestions regarding the outstanding ones. When one attempts to correlate the maze of uncontrolled and unknown variables, as encountered in such cases, the difficulty of arriving at a direct solution becomes evident. It may well be that some apparently insignificant possibility will assume greater importance when more facts are unearthed or that some combination of factors is responsible. We wish to enlist the interest of other observers in this problem. It is primarily

for this reason that these cases are reported.

#### SUMMARY AND CONCLUSIONS

- 1. Four cases of a generalized exanthem, apparently associated with localized roentgen irradiation, are reported.
- 2. The similarity of the four cases is so apparent as to suggest a distinct clinical entity with a common etiology.
- 3. Barbiturates were administered at some time in each case but evidently played no important rôle in the development of the skin lesions. The exanthems ran their similar course regardless of barbiturate intake.
- 4. Some additional factors in the causation of this exanthem are discussed.

#### REFERENCES

- ARZT, L., and FUHS, H. Roentgen Rays in Dermatology. William Wood & Co., Baltimore, 1937, p. 75.
- 2. Enfield, C. D. Sequelae of x-ray treatment. Kentucky M. J., 1937, 35, 341-344.
- 3. KAUTZKY, A. Problem of atypical skin reactions following roentgen irradiation. *Strahlentherapie*, 1937, 60, 439-443.
- MACKEE, G. M. Roentgen ray reactions and injuries. In: Clinical Roentgen Therapy, E. A. Pohle, Editor. Lea & Febiger, Philadelphia, 1938, p. 745.
- 5. Mason, V. R., Courville, C. B., and Zis-Kind, E. Porphyrins in human disease. *Medicine*, 1933, 12, 355-439.
- 6. PARDO CASTELLÓ, V. Allergic cutaneous eruptions after high voltage roentgen therapy. Arch. Dermat. & Syph., 1936, 33, 886.
- 7. Popp, W. C., and Binger, M. W. Use of pentobarbital sodium for roentgen nausea and vomiting. *Radiology*, 1937, 28, 211–214.
- 8. RICHARDS, G. E., and PETERS, M. V. Nembutal in treatment of radiation sickness. Am. J. ROENTGENOL. & RAD. THERAPY, 1936, 35, 522-525.
- 9. Trostler, I. S. Porphyrinemia and porphyrinuria; warning regarding their importance in roentgen therapy. *Radiology*, 1936, 27, 479–480.
- 10. TROSTLER, I. S. Barbiturates and irradiation. J. Am. M. Ass., 1938, 106, 1588.
- Uhlmann, E. Ueber eine durch Barbitursäurederivate ausgeloste Röntgenstrahlenreaktion. Deutsche med. Wchnschr., 1936, 62, 216–217.
- 12. Waters, C. A., and Kaplan, I. I. The 1936 Year Book of Radiology. Year Book Publishers, Inc., Chicago, 1936, p. 588.

## THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Twenty-fifth Annual Meeting: Hotel Waldorf Astoria, New York City, June 10–11, 1940.

## ∞ E D i T O R I A L S ⋈

## THE CLINICAL ASPECT OF INVOLVEMENT OF THE RETROPERITONEAL LYMPH NODES BY MALIGNANT NEOPLASMS

IN THE spreading of many malignant neoplasms, the lymphatic system as a whole, and the regional lymph nodes in particular, play such an important rôle that the manifestations arising from their involvement often completely dominate the clinical picture. In this respect, the tendency and habits of most metastases, when localized to easily accessible, as for example, the cervical, axillary or inguinal, lymph node groups are thoroughly understood. The symptoms and physical signs are as a rule found to be so well correlated with the degree of pathologic extension that one could almost speak, if it were not for the self-evident simplicity, of veritable syndromes. Even the mediastinal lymph nodes, thanks to the manifold and exacting roentgenologic methods at our disposal today, can now be easily investigated, and their invasion, either by secondary or primary neoplasms, constitutes an open problem, in most instances comparatively easy of solution. Curiously, however, little attention has been paid to the retroperitoneal lymph nodes, although because of their vast ramifications and extensive connection with organs which may form the site of many tumors, they represent perhaps the most important regional group of lymph nodes in the body.

Recently Desjardins,\* in an exhaustive article, published some very interesting observations on the clinical aspect of involvement of the retroperitoneal lymph nodes by malignant neoplasms. His study was based on the wealth of material at the

Anatomically, the retroperitoneal lymph nodes in a broader sense include the two main groups of the iliac and abdominoaortic nodes, with these latter again divided into the mesenteric and para-aortic nodes. All of them are connected by lymph channels with each other and with the individual organs. It is noteworthy that the lymph from every abdominal or pelvic organ, as well as from the lower extremities, must drain through the para-aortic or through both the mesenteric and paraaortic nodes to reach the thoracic duct and hence the left subclavian vein. A smaller amount of lymph passes into the vessels which form an anastomosis between the upper para-aortic nodes and those following the upward course of the aorta on the left side and of the inferior vena cava on the right. It must also be mentioned that the upper para-aortic nodes constitute a direct receptacle for the lymph coming in separate channels along the spermatic and ovarian arteries from the testes or ovaries, a fact which explains why malignant tumors of these organs, unless the capsule has been ruptured, first metastasize to the high abdominal lymph nodes and not to

Mayo Clinic. In a personal communication he states that in the lymphoblastoma alone the histories and case reports of not less than two thousand cases treated since 1920 were analyzed. The compilations extended over a period of nearly four years, and, therefore, considering the meticulously careful investigative nature and the arduous solicitude for the unbiased truth of the author, the results arrived at may be considered as of the utmost practical significance.

<sup>\*</sup>Desjardins, Arthur U. Retroperitoneal lymph nodes; their importance in cases of malignant tumors. *Arch. Surg.*, 1939, 38, 714-754.

the topographically closer inguinal nodes as might be supposed.

Paying due regard to these peculiarities of anatomic distribution, Desjardins distinguishes in the main three clinical forms of involvement of the retroperitoneal lymph nodes, such as metastasis from carcinoma of most pelvic organs, metastasis from tumors of the testis and ovary, and lymphoblastomatous invasion.

Metastasis from Carcinoma of Pelvic Organs. The most common organs concerned are the bladder, prostate gland, uterus and rectum. If a carcinoma originating from any of these organs spreads to the retroperitoneal lymph nodes, the chief clinical symptoms may be summed up as follows: backache, which affects mostly the lumbar region, is of a dull character and is at times relieved following roentgen irradiation; pain in the abdomen, manifesting itself either in the form of irregular attacks or of more or less regular spells occurring after meals and thus suggesting peptic ulcer; bloating and belching, usually associated with a sensation of fullness in the epigastrium after eating and in later stages with crowding of the stomach; gradually developing enlargement of the abdomen and finally persistent severe constipation. The physical signs, if not overshadowed by those of the primary neoplasm or its extension to some other abdominal organ, as, for example, the liver, consist principally of the presence of an abnormal, deepseated resistance in the epigastric or umbilical region and the complaint by the patient of a slight or moderate tenderness when pressure is exerted on this resistance.

Metastasis from Malignant Tumors of the Testis or Ovary. By far the most frequent neoplasms of the testis are the seminoma and the teratoid tumor, both types of which metastasize, according to Desjardins, much earlier than is generally suspected. As already stated, the first metastasis is almost always in the para-aortic lymph nodes, as a rule above the point of entry of the spermatic artery. Only after the tumor has broken through the capsule

of the testis is there an extension to the inguinal lymph nodes. In many instances, efficient blockage by the retroperitoneal nodes may delay further spreading of the malignant process for many months or even years. A similar situation may occur in malignant neoplasms of the ovary, although here the more rapid perforation of the capsule often changes the mode of dissemination.

The clinical symptoms in connection with metastasis to the retroperitoneal lymph nodes of the malignant tumors of the testis or ovary are identical with those described for metastasis of carcinoma of other pelvic organs. Likewise the physical signs are the same, except perhaps for the fact that the mass or resistance which is felt in the upper abdomen is more apt to be situated to the right or left of the midline, according to which side was primarily affected. Rarely there may also be retrograde extension to the iliac nodes when the malignant cells are "dammed back" by the blocking of the para-aortic lymph nodes as demonstrated in the experiments of Iamieson and Dobson.\* In malignant neoplasms of the ovary with early perforation of the capsule, the clinical picture is obscured by the signs of peritoneal dissemination such as ascites, meteorism, etc., so that a diagnosis of retroperitoneal involvement often appears difficult or impossible.

Lymphoblastoma (Hodgkin's Disease or Lymphosarcoma). It is in Hodgkin's disease and lymphosarcoma that the involvement of the retroperitoneal lymph nodes assumes the greatest clinical importance. Whether the neoplastic invasion occurs primarily or is the result of secondary extension from the cervical, mediastinal or some other lymph node groups, it invariably gives rise to symptoms or signs which sooner or later become predominant. Desjardins considers the following features as being indicative or at least suggestive of affection of the retroperitoneal lymph nodes by lymphoblastoma:

\* Jamieson, J. K. and Dobson, J. F. The lymphatics of the testicle. Lancet, 1910, 7, 493-495.

The symptoms often vary in degree from time to time and following the most varied kinds of treatment as, for example, even an erroneously performed appendectomy or cholecystectomy, they may undergo complete remission for a shorter or longer period. Their rapid deterioration, as a rule, signifies that the lymphoblastoma has invaded the structures of the throat, the mediastinum, the hemopoietic system or the retroperitoneal lymph nodes, with the latter leading in point of frequency as well as relative importance.

Individually, the most outstanding symptoms in connection with the involvement of the retroperitoneal lymph nodes by the lymphoblastoma are: the loss of strength; the unaccountable and often extremely rapid loss of weight; the slowly but more or less steadily increasing upper abdominal discomfort or pain in contradistinction to the painlessness of lymphoblastoma of other locations; the likewise continuously • increasing backache; the bloating and belching, usually greatest after eating, and sometimes associated with nausea or vomiting; the fever, which is of the Pel-Ebstein or the continuous variety, and which, more than anything else, indicates retroperitoneal (or more rarely mediastinal) invasion; and finally the pruritus which, like the fever, constitutes another positive sign.

Of the less frequent, and not altogether characteristic, symptoms one may mention the increased pigmentation of the skin, the constipation, the edema, the ascites, the jaundice and the secondary urinary disturbances.

The physical signs, according to Desjardins, are few. Moreover, they are entirely missing in the earlier stages of the involvement even in instances in which the clinical symptomatology is fully developed. Only after the lymph nodes have enlarged to a considerable size is it possible to elicit the first tangible physical evidence either in the form of solitary tumors when the nodes are individually affected, or of a deep resist-

ance when they are packed together or matted to the adjacent structures. The other worthwhile physical sign is tenderness on pressure which in most cases is quite definite, although not always unmistakable.

Roentgen examination also has a very limited usefulness. Occasionally the demonstration of a filling defect in the stomach, small intestine or colon on gastrointestinal study or of a dilated ureter and kidney pelvis on urography permits the supposition of extrinsic pressure effect, but the source as a rule remains undetermined.

Taken as a whole, it becomes evident that a knowledge of the clinical picture of the involvement of the retroperitoneal lymph nodes by malignant neoplasms is of great practical significance. Many times the array of potential symptoms may appear too long and the corresponding number of actual physical signs too small to permit an entirely lucid interpretation; nevertheless the continuous remembrance of the various possibilities will help in establishing more rational and certainly more circumspective therapeutic criteria. It thus will seem by no means unjustified to extend irradiation in all the above enumerated neoplastic conditions to the retroperitoneal lymph nodes whenever there is the slightest clinical suspicion that they may be affected or, even prophylactically, whenever there is a chance that their invasion may be reasonably prevented. On such a basis one will not hesitate, for example, to administer radiation therapy routinely to the upper abdomen in addition to other customary regions in all cases of malignant tumors of the ovary and especially the testis. Moreover, in lymphoblastoma a similar procedure, when leading to remission of unaccountable clinical symptoms such as fever, pruritus, loss of weight, etc., acquires the significance of a true differential test, both as to the probable nature and definite location of the active pathologic involvement.

T. LEUCUTIA

## AMÉDÉE GRANGER 1879–1939

DR. AMÉDÉE GRANGER, internationally famous radiologist and head of the radiological department of the Charity Hospital in New Orleans, died December 15, 1939, from a heart attack.

A native of New Orleans, Dr. Granger at the time of his death was a faculty member of the Louisiana State University Medical Center and head of the department of roentgenology at Charity Hospital, a position he had held since its creation in 1905. Dr. Granger was for many years a member of the Tulane University Medical faculty, but he became affiliated with Louisiana State University in 1931.

Famed particularly for his development of the sinus position which bears his name under the caption of the "G-line," Dr. Granger perfected many other ingenious devices for use in the roentgen examination. During the World War he was decorated by the French Government for his development of a machine to localize bullets by the aid of the roentgen ray. On other occasions he was the recipient of honors from the governments of France, Belgium and Italy.

Dr. Granger was born in New Orleans in 1879 and received his early education in private school and at the Boys' High School in New Orleans. He later attended Tulane University and was graduated from the Medical School in 1901. His study at Tulane was interrupted when he was mustered into service in the war with Spain in 1898 to serve in the Hospital Corps. In 1905, when he was appointed to organize the department of roentgenology at Charity Hospital, he was given only 169 square feet of space and one orderly. Nevertheless, he made over nine hundred roentgenograms the first year and through his guidance, this department at Charity Hospital is now one of the largest and best equipped in the country.

Dr. Granger's accomplishments were widely recognized abroad. King Albert of Belgium, through the Belgian Consul in New Orleans, made him a Knight of the Order of the Crown in 1929. In 1930, he was paid the same honor by King Victor Emanuel of Italy. In 1934, he was received into the membership of the Legion of



Amédée Granger

Honor of France. He had previously been awarded the silver and gold "Palmes Universitaires."

A past first vice-president of the Radiological Society of North America, Dr. Granger was awarded the Society's gold medal in 1926 in recognition of his achievements. He held membership in many other medical and scientific societies. He was a charter member and past chancellor of the American College of Radiology; past vicepresident of the French-speaking Physicians of North America; past president of the Orleans Parish Medical Society; honorary member of the Texas Radiological Society; honorary member of the New Orleans Ophthalmological Oto-laryngological Society; collaborator of *Radiology*; and an honorary member of the Alpha Omega Alpha medical fraternity.

Dr. Granger made many contributions to the science of radiology. The development of roentgen treatment for acute mastoiditis in children, before the softening and breaking down of bone, was the one of which he was most proud. The board of administrators of Charity Hospital gave a reception in his honor when, in 1930, he first presented a paper on this form of

treatment. This was the first time in the history of the Hospital that such an honor had been tendered a member of the Hospital staff. The devising of contrivances for improving roentgenological technique was indeed his hobby. His laboratory was filled with ingenious devices which he used for his own convenience.

Dr. Granger is survived by his wife, Corinne Pruitt Granger, whom he married in 1917, and two sons by a former marriage, Amédée, Jr., and Carroll.

He will be greatly missed in New Orleans and by the whole country. As a gentleman of extensive culture and refinement and as an acknowledged and honored scientist, he was beloved by his associates and his many friends.

ERNEST CHARLES SAMUEL

## . SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

## MEETINGS OF ROENTGEN SOCIETIES\*

United States of America

AMERICAN ROENTGEN RAY SOCIETY

Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Hotel Statler, Boston, Mass., Oct. 1-4, 1940.

AMERICAN COLLEGE OF RADIOLOGY

Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Next Annual Meeting: Commodore Hotel, New

York City, June 12, 1940.
Section on Radiology, American Medical Association Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: New York City, June 10–14,

RADIOLOGICAL SOCIETY OF NORTH AMERICA

Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting, 1940: To be announced.

RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SO-

Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

 RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September.

Section on Radiology, Illinois State Medical Society Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill. Next meeting, Peoria, Ill., May 21–23, 1940.
RADIOLOGICAL SECTION, LOS ANGELES CO. MED. Soc.
Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los

Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

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BROOKLYN ROENTGEN RAY SOCIETY

Secretary, Dr. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on first Tuesday, October to

BUFFALO RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to May inclusive at the Hotel Sherman.

CINCINNATI RADIOLOGICAL SOCIETY

Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY

Secretary, Dr. H. A. Mahrer, 10515 Carnegie Ave. Meets at 6:30 P.M. at Mid-Day Club rooms on fourth Monday each month, October to April, inclusive.

Denver Radiological Club Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY

Secretary, Dr. E. R. Witwer, Harper Hospital. Meets
monthly on first Thursday from October to May, at
Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY

Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY

Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Illinois Radiological Society

Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meetings held quarterly, on the fourth Sunday of the month.

Indiana Roentgen Society

Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis,

Ind. Meeting held the second Sunday in May annually. KENTUCKY RADIOLOGICAL SOCIETY

Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville. Meets annually in Louisville on third Sunday afternoon in April.

LONG ISLAND RADIOLOGICAL SOCIETY

Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

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Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing. Three meetings a year, Fall, Winter, Spring. MILWAUKEE ROENTGEN RAY SOCIETY

Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis. Meets monthly on first Friday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY

Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

NEBRASKA RADIOLOGICAL SOCIETY

Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY

Secretary, Dr. W. J. Marquis, 198 Clinton Ave., Newark. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by president.

NEW YORK ROENTGEN SOCIETY

Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY

Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse.

Three meetings a year—January, May, November. Pacific Roentgen Club

Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY

Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Next annual meeting, Hershey Hotel, Hershey, Pa., May 17-18, 1940.

PHILADELPHIA ROENTGEN RAY SOCIETY

Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY

Secretary, Dr. H. W. Jacox, 4800 Friendship Ave., Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y. Secretary, Dr. S. C. Davidson, 277 Alexander St. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

ST. LOUIS SOCIETY OF RADIOLOGISTS

Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY

Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

<sup>\*</sup> Secretaries of Societies not here listed are requested to send the necessary information to the Editor

SOUTH CAROLINA X-RAY SOCIETY

Secretary, Dr. Hillyer Rudisill, Jr., Roper Hospital, Charleston. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY

Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY Secretary, Dr. L. W. Baird, Scott and White Hospital, Temple, Texas. Next annual meeting, January 18, 1941,

Sherman, Texas.

University of Michigan Department of Roentgen-OLOGY STAFF MEETING

Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00-5:00 P.M., Room 301, Service Memorial Institute.

VIRGINIA RADIOLOGICAL SOCIETY Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

WASHINGTON STATE RADIOLOGICAL SOCIETY

Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday of each month at the College Club, Seattle.

#### CUBA

SOCIEDAD CUBANA DE RADIOLOGIA Y FISIOTERAPIA Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

#### BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY

Meets monthly on third Thursday, from November to June inclusive, at 8:15 p.m., 32 Welbeck St., London. Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)

Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, I, Wimpole St., London, W. I.

FACULTY OF RADIOLOGIST.

land. Meets annually.

Secretary, Dr. Barbara M. Key, 32 Welbeck St., London,

W. 1, England. SECTION OF RADIOLOGY AND MEDICAL ELECTRICITY, AUS-TRALASIAN MEDICAL CONGRESS

Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association

Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive for scientific discussion.

Canadian Association of Radiologists

Secretary, Dr. A. C. Singleton, Medical Arts Bldg.,

Toronto, 5, Ontario.
Section of Radiology, Canadian Medical Association Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S. RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL

ASSOCIATION Secretary, Dr. Colin Anderson, Invercargill, New Zea-

#### CONTINENTAL EUROPE

BELGIAN SOCIETY OF ROENTGENOLOGY Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium). Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France

Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris. Société Suisse de Radiologie (Schweizerische Rönt-GEN-GESELLSCHAFT

Secretary for French language, Dr. A. Grosjean, La

Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale

Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radi-OLOGISTS IN CZECHO-SLOVAKIA Secretary, Dr. Walter Altschul, German University,

Prague, 11.52.

DEUTSCHE RÖNTGEN-GESELLSCHAFT (GESELLSCHAFT FÜR RÖNTGENKUNDE UND STRAHLENFORSCHUNG)

Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.

Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

SÜD- UND WESTDEUTSCHE RÖNTGENGESELLSCHAFT Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft

Meets annually in different cities.

DUTCH SOCIETY OF ELECTROLOGY AND ROENTGENOLOGY Holds two meetings a year in Amsterdam, one in the

spring, and one in the fall.
Societa Italiana Radiologia Medica

Secretary, M. Ponzio, University of Turin, Prof. Turin SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.

Secretaries, Drs. S. A. Reinberg and S. G. Simonson.

Meets annually.

LENINGRAE ROENTGEN RAY SOCIETY Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad. Moscow Roentgen Ray Society

Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly on first Monday at 8

POLISH SOCIETY OF RADIOLOGY

Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology Secretary, Dr. B. Krynski, 11 Zielna St. Meets once a month except in the summertime.

SCANDINAVIAN ROENTGEN SOCIETIES The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

SOCIETY OF MEDICAL RADIOLOGY IN SWEDEN Meets in Stockholm.

SOCIETY OF MEDICAL RADIOLOGY IN NORWAY Meets in Oslo.

Society of Medical Radiology in Denmark

Secretary, Dr. G. Biering, Copenhagen. Meets the second Wednesday of each month from October to July in Copenhagen, at 8 'oclock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland Meets in Helsingfors.

VIENNA ROENTGEN SOCIETY

Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

#### ORIENT

JAPAN X-RAY ASSOCIATION c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

KINKI ROENTGEN-ABEND SOCIETY Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto,

#### AMERICAN COLLEGE OF RADIOL-OGY ANNOUNCES PRO-FESSIONAL BUREAU

In 1937 the American College of Radiology started operation of a placement bureau in an effort to bring together those radiologists who were looking for locations and those hospitals and medical groups who were seeking radiologists. This bureau was started as an experimental venture in order to determine whether or not there was need for such a service. During the experimental period very little publicity was given to the availability of such a service. but even without publicity the placement bureau has been able to offer its facilities to approximately seventy applicants and institutions. Likewise, it has aided individual radiologists who sought a well trained associate to take care of an expanding practice.

Prior to the establishment of the placement bureau it had been the custom of hospitals to write to a few medical centers which were training radiologists and ask if any well trained man was available. If none was obtainable they were forced to consult one institution after another until a satisfactory man was found. Another source of obtaining radiologists was through the commercial bureaus.

At the recent annual meeting of the Board of Chancellors of the American College of Radiology it was deemed advisable to expand the activities of the placement bureau and make it a truly Professional Bureau. At the present time a full biography including college and medical training, period of interneship, and residency, is being compiled for all applicants. Each hospital, or group, or individual requesting a radiologist is asked to furnish detailed information pertaining to the nature of the practice. If a hospital, it is queried concerning size, population of the community, equipment, and other pertinent facts about its radiological depart-

The applicants are requested to state whether or not they are diplomates of the

Board of Radiology and to specify their period of training in order that it may be determined whether or not they are to be potential candidates for the Board examinations. The Professional Bureau accepts as applicants only those who have had sufficient training to be candidates for the Board or those who have been awarded certificates by the Board. (The Bureau does not undertake to place residents or to find locations for those men desiring to enter training; nor does it endeavor to furnish technicians.)

At the present time there are eightyeight approved radiological centers training one or more men. It is the plan that when a request is received all applicants and the chief of the department in which each man received his training will be notified of the opening. The men are requested to write to the individual or institution for further information and also to furnish the credentials requested. This method of procedure is followed because of the fact that each opening calls for different requirements and by going over the credentials of the applicants the inquirers can select those whom they feel meet their particular needs. The Professional Bureau acts in an advisory capacity between the institution and the applicant and intends to make every attempt to obtain the additional information necessary for each party.

Up to the present time no charge has been made to either applicant or hospital for services rendered. It is evident that the expense to be incurred by the College in the operation of such a Professional Bureau is rather difficult to estimate at the present time, and all expenses are now being borne by the College. It has been decided that if and when the operation of the Bureau is sufficiently large to incur considerable expense from which only the applicants will benefit, then a small registration charge will be made.

All hospitals, groups, clinics, and individuals, seeking the service of a radiologist or an assistant in the radiological de-

partment are invited to communicate with Dr. S. W. Donaldson, Director of the Professional Bureau, American College of Radiology, 540 North Michigan Avenue, Chicago.

#### AMERICAN RADIUM SOCIETY

The Twenty-fifth Annual Meeting of the American Radium Society will be held in New York City on Monday and Tuesday, June 10 and 11, 1940, at the Hotel Waldorf Astoria.

The Janeway Lecture will be given by Dr. Edith H. Quimby on Monday afternoon at four o'clock on the subject "The Specification of Dosage in Radium Therapy." Formal presentation of the Janeway Medal will be made at the dinner on the evening of the same day.

A clinical demonstration at Memorial Hospital has been arranged for Wednesday afternoon, June 12, and a visit to the cyclotron at Columbia on Thursday afternoon, June 13, to avoid conflict with the Section on Radiology of the American Medical Association which will be in session during the mornings on these days. Members who have not obtained hotel reservations should do so promptly.

## EIGHTH AMERICAN SCIENTIFIC CONGRESS

The Department of State announces that the Eighth American Scientific Congress will be held in Washington, D. C., from May 10 to 18, 1940, under the auspices of the Government of the United States.

Pursuant to a special act of the Congress of the United States invitations on behalf of the President have been extended to the Governments of the American Republics members of the Pan American Union to participate in the forthcoming meeting. Scientific institutions and organizations are also cordially invited to send representatives.

On April 14, 1940, the Pan American Union will celebrate the fiftieth anniversary of its founding. Although the

Eighth American Scientific Congress will convene a few weeks subsequent to the anniversary date, the Congress will be one of the important phases of that notable celebration.

The Congress will be divided into the following sections, each to be in charge of a chairman assisted by a vice chairman, secretary and section committee: anthropological sciences; biological sciences; geological sciences; agriculture and conservation; public health and medicine; physical and chemical sciences; statistics; history and geography; international law, public law and jurisprudence; economics and sociology; education.

The official languages of the Congress will be English, Spanish, Portuguese and French. Papers may be submitted in any one of the official languages and appropriate arrangements will be made for the presentation of these papers, or résumés thereof, in the other official languages.

The Honorable Cordell Hull, Secretary of State, has requested the following government officials and distinguished scientists to serve upon an Organizing Committee which is collaborating with the Department of State in formulating definite plans for the Congress:

The Honorable Sumner Welles, Under Secreary of State, *Chairman*.

Dr. Warren Kelchner, Acting Chief, Division of International Conferences, Department of State, *Vice Chairman*.

Dr. Alexander Wetmore, Assistant Secretary of the Smithsonian Institution, Secretary and Secretary General of the Congress.

Dr. C. G. Abbot, Secretary of the Smithsonian Institution.

Dr. Isaiah Bowman, President, John Hopkins University.

Dr. Vannevar Bush, President, Carnegie Institution of Washington.

Dr. Ben M. Cherrington, Chief, Division of Cultural Relations, Department of State.

Mr. Laurence Duggan, Chief, Division of the American Republics, Department of State.

Dr. Ross G. Harrison, Chairman, National Research Council.

Dr. Waldo G. Leland, Secretary, American Council of Learned Societies. Mr. Archibald MacLeish, Librarian of Congress.

Dr. Thomas Parran, Surgeon General, United States Public Health Service.

Dr. Stuart A. Rice, Chairman of the Central Statistical Board.

Dr. Leo S. Rowe, Director General, Pan American Union.

Dr. James Brown Scott, Trustee and Secretary, Carnegie Endowment for International Peace.

#### RED CROSS TO ENROLL MEDICAL TECHNOLOGISTS

At the request of the Surgeon General of the Army and in compliance with its policy of cooperation with both the Army and Navy, the American Red Cross, as an expansion of its peace-time service for the military forces, has undertaken the enrollment of various types of medical technologists who are willing to serve in the medical department of the Army and Navy if and when their services are required at the time of a national emergency.

Persons with the following qualifications will be enrolled:

Chemical laboratory technicians (male) Dental hygienists (male and female)

Dental mechanics (male)

Dietitians (male and female)

Laboratory technicians (male and female)

Meat and dairy hygienists (inspectors) (male) \*Nurses (male)

Occupational therapy aides (male and female) Orthopedic mechanics (male)

Pharmacists (male and female)

Physical therapy technicians (aides) (male and female)

Statistical clerks (male and female)

X-Ray technicians (male and female)

General qualifications for enrollment are as follows:

- 1. Citizens of the United States.
- 2. Ages 21-45 years (Army); 18-35 (Navy—men only)
- 3. Physically qualified. Applicants must pass a satisfactory physical examination, according to standards set respectively by the Army and Navy Medical Departments.

- 4. Women applicants must be unmarried.
- 5. All applicants must express a willingness to serve as a technologist in time of a national emergency.

Male technologists will be eligible for enlistment in the Army as non-commissioned officers in the grades of sergeant, staff sergeant, or technical sergeant. Women technologists, and men who do not qualify physically, will be eligible for employment by the Army as civilians.

For the Navy, male technologists will be eligible for enlistment in the Naval Reserve as Petty Officers—Pharmacist's Mates 3d, 2nd, and 1st Class and Chief Pharmacist's Mate (acting appointment). Women technologists are not eligible for service in the Navy under present plans.

The Medical Department of the Army will require a considerable number of technologists in each of the above named groups. The Navy Medical Department requirements will be similar except for dietitians, occupational therapy aides, orthopedic mechanics and dairy and food hygienists (inspectors) who will not be needed. Notwithstanding the maintenance of this enrollment, the Navy also desires peace-time enlistment in the U. S. Naval Reserve, and male technologists who wish to enlist in the Naval Reserve are urged to communicate direct with the Commandant of the Naval District in which they reside. The address of their Commandant will be furnished upon request.

Technologists who qualify according to these general standards and who are willing to enroll for service as outlined above should communicate with the American National Red Cross, Washington, D. C.

# CALCIFICATIONS IN THE SPLENIC REGION

To the Editor:

A short time ago I had the occasion to recheck some of the autopsy material used in the preparation of my paper (Calcifications in the Splenic Region. Am. J. ROENT-GENOL. & RAD. THERAPY, June, 1939, 41, 931–949) in collaboration with several

<sup>\*</sup> This group will not be members of the Army or Navy Nurse Corps which under basic law are limited to females, but will be used as technologists for service auxiliary thereto.

members of the Department of Pathology at Mt. Sinai Hospital, New York City.

Three cases of splenic phleboliths were originally found in the autopsy protocols of the above mentioned hospital and reported as such in the article. Careful microscopic re-examination of representative sections of two of these spleens failed to demonstrate the calcific bodies lying in or

intimately connected with blood vessels. In the third case histological study of the splenic calcification was not made.

Therefore, in the interests of accuracy, I should like to alter the position of the three cases originally presented as splenic phleboliths to that of calcifications of undetermined origin.

ARNOLD L. BACHMAN



#### BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

Chronic Arthritis in Wild Mammals. By Herbert Fox, Professor of Comparative Pathology, University of Pennsylvania; Director, William Pepper Laboratory, Hospital of the University of Pennsylvania. Transactions of the American Philosophical Society Held at Philadelphia for Promoting Useful Knowledge. New Series—Volume XXXI, Part II. Paper, \$2.00, per volume. Pp. 73–149, with numerous illustrations. Philadelphia: The American Philosophical Society, 1939.

This monograph is an analysis of more than seventeen hundred skeletons and autopsies of wild animals of which some revealed changes in the joints that correspond with those of chronic arthritis in man. The material was obtained from the autopsy service at the Zoological Garden, Philadelphia, from museums and from wild animals which were killed by naturalists on expeditions and by hunters. In 1,749 skeletons, 77 cases of arthritis were found.

The introduction to the monograph contains a statement of the intention and the plan of the work, a description of the sources of the material, a definition of arthritis as applied to wild animals and a discussion of the limitation of the material and of the value of roentgen examination of the bones. Following this is a table which lists the skeletons of the animals and the autopsies performed on them, arranged according to zoological classification with common names of the principal examples. The anatomical characteristics of the articular changes in each class are fully described in tabulated form. In the concluding paragraphs the ecology and habits of the various groups, the associated morbid states and the relationship of diet, age and body bulk to arthritis are discussed.

The illustrations are profuse and are very clear with excellent detail of both autopsy specimens and roentgenograms. The latter were submitted to trained roentgenologists and the readings which are given are in accord with their interpretations. Evidences of hyperostotic overgrowth, osseous solidifications, porosis and surface defects which are present, are com-

parable to those observed in roentgen examination of human joints. Dr. Fox believes that chronic arthritis can be well demonstrated in wild animals by roentgen examination and the findings which are obtained amplify and support the interpretations of the gross specimens by the pathologist.

Arthritis was best seen as an involvement of the spinal column but it also occurred very extensively in the appendicular skeleton. The distributions of the lesions in different kinds of animals suggested that a relationship may exist between function and localization of disease. Thus locomotion and the jolt shock associated with it may be a factor in its production. Macrosomic animals were found to be conspicuously affected; small bodied animals, rodents, bats, etc., were free from lesions. No apparent relationship between arthritis and taxonomic position, zoogeography, ecology, habits, diet, pathological panels and focal infection could be discovered. The varieties which had the most pronounced lesions were the anthropoid apes and baboons. Lesions were found not only in specimens exhibited in menageries but also in the material that was in its proper habitat when killed.

This monograph which is the result of painstaking observation and research is well worth study by roentgenologists and physicians and should be in the library of all those especially interested in the problem of arthritis, its etiology and pathology.

R. S. Bromer

DIE RÖNTGENTIEFENTHERAPIE. Unter Mitarbeit von Fachgenossen zusammengestellt von Professor Hans Holfelder, O. Ö. Professor für allgemeine klinische Röntgenkunde an der Johann-Wolfgang-Goethe-Universität, Frankfurt A. M. Paper, price RM. 27; bound, price RM. 29. Pp. 341, with 264 illustrations. Leipzig: Georg Thieme, 1938.

This book, written partly by Holfelder and partly by several collaborators including Beutin, Englmann, Reisner, Töppner, Bulich, Engels, Teschendorf and others, is well printed on good paper and contains numerous and effective illustrations. It constitutes an excellent description and discussion of the ideas and methods of Holfelder and his school. Therefore, it will be of interest to all radiologists who are interested in familiarizing themselves with these ideas and methods. In no way can it be regarded as a thorough discussion of all phases of radiotherapy, because a number of conditions have not been included at all or have only been mentioned incidentally. Especially interesting perhaps are Englmann's chapter on the microscopic changes following irradiation, and the chapter by Reisner and Holfelder on skin reaction and the rhythm of irradiation, as well as Teschendorf's chapter on roentgen irradiation and its effect on offspring.

A. U. Desjardins

A HISTORICAL CHRONOLOGY OF TUBERCULOSIS. By Richard M. Burke, M.D., State Veterans Hospital, Sulphur, Oklahoma. Cloth. Price, \$1.50. Pp. 84. Springfield, Illinois: Charles C Thomas, 1938.

This small book follows the subject of tuberculous infection from 5000 B.C. to the present.

If one is interested in knowing who did what and in what year then the purpose of the volume has evidently been fulfilled. It seems to the reviewer that any chronology should at the same time be supplemented with a bibliography of the events recorded; otherwise, the effort becomes a mere maze of dates which, without adequate knowledge of the significance of such dates, leaves the reader little improved. A chronology of any disease with an adequate accompanying bibliography would be of great value.

The authors have divided the book into an Ancient Period (5000 B.C.-1600 A.D.); a Premodern Period (1600-1800); and a Modern Period (1800——).

It would appear to the reviewer that nothing of significance happened in the year 1800 to herald it as the natal day of the modern era. Aside from the then and now little realized value of Laennec's contributions, little of real worth in our knowledge of tuberculous infection happened until 1882. It then took twenty-two more years to find a suitable method of therapy, and it appears to the reviewer that not until the nineteen twenties did the modern period truly begin. It was during these years that our knowledge of the pathology, chemistry, and therapy of tuberculosis really advanced. The latter portion of the book lags markedly in its

recording of the great advances made in case findings and collapse therapy, and these must be considered as some of the foremost steps in any chronological record of tuberculosis.

It seems to the reviewer that such a compilation of dates without an accompanying bibliography is of interest only to the occasional reader and that it can serve no real purpose in the advancement of our knowledge of tuberculosis in the manner in which it should be advanced.

WILLIAM M. TUTTLE

The Physiology of Exercise: A Text-Book for Students of Physical Education. By James Huff McCurdy, A.M., M.D., M.P.E., Director of Physical Education, Springfield College, Springfield, Mass., etc., and Leonard A. Larson, B.A., B.P.E., M.Ed., Ph.D., Professor of Health and Physical Education, Springfield College, Springfield, Mass. Third edition, thoroughly revised. Cloth. Price, \$3.75, Pp. 349. Philadelphia: Lea & Febiger, 1939.

This is the third edition of the present book; the dates of the first two editions are not given. Two new sections have been added: (1) a chapter on exercise for persons over forty years of age, and (2) a section on exercise for women. The authors deal interestingly with the purposes of physical exercise in the various age groups, reviewing the physiological and chemical aspects as well as the general effects of physical effort. In considering the effects of exercise upon the heart it is stated that the hearts of successful marathon runners as larger than average and that enlargement occurs immediately following a marathon race. Differing with this observation are the studies of Levine and others. They found that the hearts of the majority of marathon runners were remarkably normal as to size, and immediately following a race the hearts were actually smaller and remained so for approximately two hours before returning to their previous size. The book is interesting and practitioners should find in it considerable material of great value, particularly for the guidance of young persons and those above the age of forty.

Burgess Gordon

THE LIFE OF CHEVALIER JACKSON: AN AUTO-BIOGRAPHY. Cloth. Price, \$3.50. Pp. 229, with many plates. New York: The Macmillan Company, 1938.

This is indeed a most interesting account of

a most interesting and useful life. The book deals with the entire remembering years of the author. It traces admirably the early years of his practice, of the gradual interest and development of endoscopy. It relates the rise of a new type of medical endeavor in this country.

Certainly no man has done more to bring forth a new science within the science of general medicine. The story of this long course is told in the book. Such advances are not made in the short period of a year but through many years, and it seems to the reviewer that this is the real message that the book has to bear. It should give courage to those entering new fields and bring them to realize that there is much to do and that it can be done even though the beginnings are humble.

In parts, the book may give the impression that the author has dealt too fully with personal feelings and reactions, especially with those opinions which were fostered in the early years of life. It is the prerogative of all, however, to have such memories, and the relating of them the special prerogative of those who by their life work have attained a niche among the great in any field.

The work is well done and an inspiration, and the life portrayed a goal to those who view fine endeavor as something removed from the field of medicine. It again reveals that a science within a science can still be created.

WILLIAM M. TUTTLE

#### BOOKS RECEIVED

Principles of Roentgenological Interpretation. By L. R. Sante, M.D., Professor of Radiology, St. Louis University School of Medicine; Radiologist to St. Louis City Hospital and St. Mary's Hospital, St. Louis. Third Revised Edition. Cloth. Pp. 340, with 333 illustrations. Ann Arbor, Michigan: Edwards Brothers, Inc., 1940.

RADIODIAGNOSTICO. TOMO I. FISICA DE LOS RAYOS X APARATOS. By Gonzalo Esguerra Gomez, Profesor en la Facultad de Medicina de la Universidad Nacional. Cloth. Pp. 115, with 80 illustrations. Bogota, Colombia, S. A., 1938.

RADIODIAGNOSTICO. TOMO II. SISTEMA OSEO. By Gonzalo Esguerra Gomez, Profesor en la Facultad de Medicina de la Universidad Nacional. Cloth. Pp. 335, with 400 illustrations. Bogota, Colombia, S. A., 1939.

LA ROENTGENCHIMOGRAFIA CARDIO-VASCO-LARE. By Prof. Pietro Perona, Incaricato di Radiologia nella R. Universita di Padova. Paper. Pp. 356, with 169 illustrations. Belluno: Casa Editrice Libraria A. Salvador, 1939.

HEPATOLIENOGRAPHIE MIT JODSOL. Von Dr. Franz Beckermann, Sedkundärarzt der I. medizinischen Klinik der Hansischen Universität. Cardboard. Price, RM. 8. Pp. 88, with 65 illustrations. Leipzig: Georg Thieme, 1940.

DAS BRUSTBEIN UND SEINE GELENKE: NOR-MALE UND KRANKHAFTE BEFUNDE, DARGE-STELLT ZUM TEIL MITTELS NEUER RÖNTGEN-OLOGISCHER METHODEN. (Fortschr. a. d. Geb. d. Röntgenstrahlen, Ergänzungsband 58.) Von Dr. E. A. Zimmer, Assistent am Röntgeninstitut der Universität Basel. Paper, price RM. 13; bound, RM 15. Pp. 70, with 81 illustrations. Leipzig: Georg Thieme, 1939.

CANCER HANDBOOK OF THE TUMOR CLINIC, STANFORD UNIVERSITY SCHOOL OF MEDICINE. Edited by Eric Liljencrantz, M.D., Chief of Tumor Clinic, Stanford University School of Medicine, Consultant in Neoplastic Disease, United States Naval Hospital, Mare Island, and United States Marine Hospital, San Francisco. Cloth. Price, \$3.00. Pp. 114, with 50 illustrations. California: Stanford University Press, Stanford University, 1939.

Medical Uses of Radium. Summary of Reports from Research Centres for 1937. Paper. Price, 35 cents. Pp. 48, with 5 illustrations. Medical Research Council, Special Report Series, No. 232. London: His Majesty's Stationery Office, 1938. (May be obtained from British Library of Information, 50 Rockefeller Plaza, New York.)

Medical Uses of Radium. Summary of Reports from Research Centres for 1938. Paper. Price, 30 cents. Pp. 49, with 5 illustrations. Medical Research Council, Special Report Series, No. 236. London: His Majesty's Stationery Office, 1939. (May be obtained from British Library of Information, 50 Rockefeller Plaza, New York.)

WIDE FIELD X-RAY TREATMENT: THE VALUE OF THE X-RAY BATH METHOD IN DISEASE AND HEALTH. By S. Gilbert Scott, M.R.C.S.,

L.R.C.P., F.F.R., D.M.R.&E. (Camb.), Consulting Radiologist to the London Hospital; Honorary Radiologist to the British Red Cross Rheumatism Clinic, London: Honorary Physician Radiologist to the Charterhouse Rheumatism Clinic. Cloth. Price, 8/6. Pp. 80, with 13 illustrations. London: George Newnes Limited, 1939.

Annual Report on the Results of Radio-Therapy in Cancer of the Uterine Cervix. Third Volume. Statements of Results Obtained in 1932 and Previous Years (collated in 1938). Edited by J. Heyman, M.D., Stockholm. Paper. Pp. 149, with numerous tables. League of Nations Health Organisation. Official No. C.H. 1427. Geneva, 1939.

A Textbook of Surgery. By John Homans, M.D., Clinical Professor of Surgery. Compiled from lectures and other writings of members of the Surgical Department of the Harvard Medical School. Fifth edition. Cloth. Price, \$8.00. Pp. 1272, with 530 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

REPORTS ON MEDICAL PROGRESS, 1939, as Published in the New England Journal of Medicine. Compiled and Edited by Robert N. Nye, M.D. Cloth. Price, \$5.00. Pp. 562. Boston: Little, Brown and Co., 1940.

DIE BIOLOGISCHE REAKTION: EINE FUNKTIONELLE ANALYSE UND SYNTHESE BIOMETRISCHER WERTE ZUR ZAHLEMÄSSIGEN ERFASSUNG VON: ALLERGIE; ALLGEMEINER RESISTENZ; SPEZIFISCHER RESISTENZ; KRANKHEITSINTENSITÄT; EXTENSITÄT AKTIVER HERDE; IMUNITÄT. VON Dr. O. H. Bucher, Leiter des Schweiz. Antituberkulose-Institutes und der Klinik Satis in Seon, und Dr. C. C. Hofflin, Victoria, B. C. Cloth. Price, fr. 42.80 or RM. 25.70. Pp. 263, with 333 illustrations. Bern: Hans Huber, 1939.

THE MEDICAL CAREER, AND OTHER PAPERS.
By Harvey Cushing. Cloth. Price, \$2.50.
Pp. 302. Boston: Little, Brown and Co., 1940.

Symposium on the Synapse. By Herbert S. Gasser, Joseph Erlanger, Detlev W. Bronk, Rafael Lorente de Nó, Alexander Forbes. Cloth. Pp. 361–474. Springfield, Illinois: Charles C Thomas, 1939.



#### DEPARTMENT OF TECHNIQUE

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# A NEW FILM ENVELOPE WITH ACCESSORY TRANSPARENT ENCLOSURE FOR ROENTGENOLOGIC REPORTS\*

By WALTER W. FRAY, M.D., M.S., and LA VERNE L. NOLAN ROCHESTER, NEW YORK

THE filing of roentgen-ray films and records has long been a problem to roentgenologists, particularly to those in hospital practice where space requirements prevent indefinite storage of films and records. The addition of new storage spaces, even if available within the hospital, does not furnish a solution, since their storage at more remote places necessitates increased labor cost.

The use of microfilm will furnish a transcript of the written or typewritten material, but it is doubtful if it represents an adequate solution to the permanent storage of roentgen-ray films. Our experience has shown that much of the finer detail is lost on any attempt at reproduction photographically of roentgenographic detail, particularly of fine lung or bone structure. It is possible that courts may finally accept such reproduced records of roentgenograms on the basis of decisions that the eye of the camera does not lie, but it should be remembered that compensations courts (in New York State) at the present time require the preservation of original films for five years. The manner in which an individual, either with or without intent to deceive, may modify his photographic technique to delete a fine fracture line of a bone or a fine linear fibrosis of the lung is appreciated by roentgenologists and photographers alike.

It becomes apparent that the original

roentgenograms and particularly the original typewritten records of roentgen reports will be desired by the roentgenologist for review when the patient returns to the department for additional examinations. This will necessitate retention of original records over long periods, the length of time being dependent mainly upon the amount of space available and the legal requirements of the state or locality.

The immediate day by day problem of handling these records by different systems of filing has varied greatly in different departments of radiology. Many systems with which we are familiar require separate files for films, for index of names, and for requisitions and reports. Because of the multiplicity of files, a large storage space is required. Attempts have been many to reduce this filing space by combining files, but usually such attempts are at least partial failures, because the actual cubic content of the files is not greatly reduced. The simple transfer of the contents from one file and their subsequent storage of the envelopes and folders combined with reports in another file cannot aid, unless the second file not only is smaller but its contents remain unfolded. Folding has the further disadvantage that for its subsequent review time is lost in locating the proper report or record.

We have tried to solve the main problems attending filing of roentgen reports,

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requisitions, and films with the following ends in mind:

- (1) To reduce the amount of filing space required to the absolute minimum.
- (2) To permit the reviewing of old or previous roentgen-ray records of the patient with dispatch, saving the time of the roentgenologist during the routine period of the interpretation.
- (3) To simplify the office procedure, thereby sparing the office personnel as much as possible of the labor burden.
- (4) To effect economies in the overhead costs of routine work if possible, or at least to accomplish the above ends without increasing costs.

These ends we feel have been accomplished by devising a special double envelope—really a single envelope with accessory flat pocket—with a transparent window permitting the reading of the entire average roentgenologic record of the patient at a glance. The films are kept within the main envelope, while the typewritten reports appear in chronological sequence and can be read or reviewed without their removal. The secretary removes them only to add new reports. A carbon copy is preferably obtained at the time of the typing, the width of the paper conforming with the size of the history sheets of the main hospital record. The paper upon which the copy is made should be of heavy index stock to permit its easy insertion into the pocket. (The original is usually desired for the medical record.) If the original is pasted into the medical record (such pasting is undesirable, since it doubles the thickness of the record sheet and triples it if pasting is employed on both sides, and in addition, throws the sheet into undulatory folds and wrinkles which greatly increases the bulk of the medical record), the width of the glued sheet should be standard in width to utilize the full width of the medical record sheet. If the films leave the division of radiology, the typewritten copy is removed from the pocket and is left in the file in proper numerical sequence to indicate the removal of the films. No additional work is required except to make a notation on this record indicating date and the destination, or person to whom the films were sent. On return of the films a notation of their return is made, the typewritten copy is inserted back in the pocket, and the filing becomes complete with minimum effort. This method of handling loaned films is preferable to a separate small file of slips. This method, in our opinion, results in the commission of two errors:

- (1) The slip is not made out in a busy department directly at the time of the loan due to the impact of other work, though the individual may have the best of intentions.
- (2) The films are often returned during the evening or at other hours when the regular personnel is not present; hence the loan slips are not removed from the small file. Subsequent inquiry for these films will bring forth the misinformation that they have been loaned, and this has caused endless confusion with us, since the inquirer starts a fruitless tour of the hospital while the films are actually within the division of radiology, either stacked unfiled in the office or filed in the main file.

The commission of such errors is avoided with the system being described, since a visit to the main file will reveal either the entire envelope with the films, etc., or the typewritten reports with information in regard to the location of the films.

The routine in handling a request for examination proceeds as follows:

The intern fills out his request for examination, which to conserve space, utilizes the heading of the roentgenologic sheet for the medical record. On receipt of this sheet together with the appointment slip in the department of radiology the case is scheduled, after checking that it is a new case without previous examinations and that the name and unit number are correctly given.

Considering the patient a new one without previous record in the department, no index cards from the file need be typed—

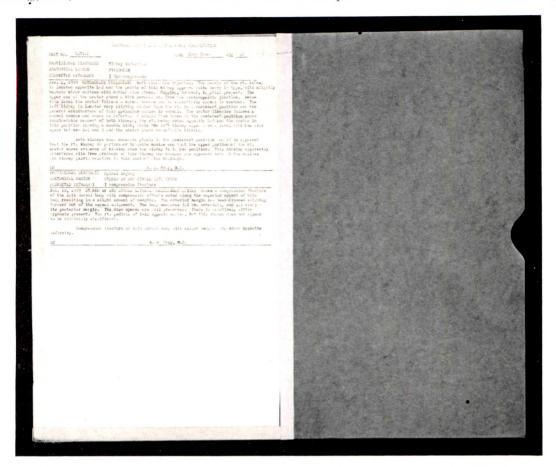


Fig. 1. Special envelope for 14 by 17 inch films showing enclosure for roentgenologic reports. The transparent front of cellophane (invisible in illustration) permits direct inspection of reports without their removal. These reports are typed in chronological sequence so that one may follow the progression of a lesion or disease without consulting and rearranging miscellaneous reports. The transparent enclosure shown in this illustration is on the left side of the envelope. By the manufacture of envelopes with either right or left enclosures, it is possible to arrange the file so that all even numbered cases have the enclosure on one side (left) and all odd numbered cases on the other (right). By this simple means, the number of film-numbers the eye must follow to find the desired one is reduced to one-half.

no additional hospital form need be filled out; the patient is simply scheduled for examination after the check shows that the case is a new one. Not even the envelope for the roentgenograms need be written upon. There is no need for name, unit, number, title of examination or date. When the films have been secured and dried, these are placed with a new folder, and the roentgenologic sheet for the medical record is slipped into the transparent pocket, and since this record sheet has already been checked for correct name and number, no further work is required until the time for interpretation.

When the film is interpreted, the secretary types the roentgenologic report on the medical record sheet, securing a carbon copy on the heavy sheet of paper with which the envelope comes supplied. The headings on the two sheets are so arranged mechanically with the carbon paper that the name and unit number appears on the copy. The type of examination, date, and type of case (O.P.D., private, Ward A, etc.) are typed in the first available line, and the report immediately follows.

If the case is an old one (one who has had previous roentgenologic examinations), the routine is even easier. The envelope for films and reports is examined (checking of spelling and unit number is not required for correctness). No typing or writing is necessary on the envelope proper at the time of the arrival of the patient. When the films are interpreted, the report follows immediately after the last interpretation, conserving all possible space. Not only is this system simple for the clerks and secretaries to handle but it is evident that the work of the roentgenologist is greatly facilitated. He has at hand, without any manipulating, all previous reports on the patient ready for his inspection at a glance, visible through the transparent window.

#### SUMMARY

Common methods now in use require individual requisitions, index card systems for name, sequence systems for numbers, stamping or writing of data on the envelope containing films, and separate individual reports on interpretations. Each of these employ repetitious use of the name, date, unit number, etc. Records in many cases will show that the name of the patient has

been written or typewritten a dozen or more times in caring for the record of a single patient who has had a succession of examinations.

To conserve time, labor, and stationery, but particularly to consolidate data and permit easy inspection of reports as well as to effect economies in storage space, a new envelope has been devised which is simple to use, spares the personnel, prevents many of the errors continually arising within the department and decreases the possibilities of loss of film or record. The few cents increase in cost of the envelope is more than offset by the saving in labor cost and economies in making and maintaining the records. Costs of stationery (requisitions, gummed paper, . envelopes, and folders) should be reduced. These savings should be of importance to the hospital administration. The roentgenologist will be interested not only in these savings but will profit greatly by the expedition and ease with which his work at interpretation will be facilitated.



#### ROENTGENOLOGIC DEMONSTRATION OF BLADDER PATHOLOGY

By J. SYDNEY RITTER, M.D., and LEO A. SHIFRIN, M.D. NEW YORK CITY

THE introduction of the roentgen ray as an aid in establishing diagnoses in diseases of the urogenital tract materially decreased the need for instrumental procedures. The use of intravenous urography and cysto-urethrography has reduced manipulations to a minimum. To further eliminate as much as is possible prolonged instrumental studies, and to exclude these practices in debilitated patients, we have resorted to the following procedure:

First, the patient voids, emptying the bladder of as much of its urine content as possible. Under strict aseptic conditions, a No. 10 or No. 12 French soft rubber catheter is passed into the bladder and an estimation of the residual urine is made. The bladder capacity is now determined by means of sterile saline and the bladder again emptied. Then a quantity of air equivalent to one-half of the bladder capacity is injected into the bladder and the catheter removed.

The patient is now given an intravenous injection of diodrast and roentgen exposures of the urinary tract are made in the usual manner. As the dye is secreted from the kidney and enters the bladder, visualization of infiltrative masses such as neoplasms or diverticula are readily demonstrated.

Figure 1 shows a large intravesical intrusion of the mid lobe of the prostate in a patient, aged seventy-four, who had an acute prostatitis due to repeated manipulations prior to his reporting to our service.

A diagnosis of marked intravesical prostatic hypertrophy was definitely estab-

lished in this case. This figure is shown merely to illustrate the results obtained by this procedure. The kidneys, ureters and bladder are outlined with a clearer picture of the bladder infiltration.

We have been able to establish a definite



Fig. 1.

diagnosis without instrumentation in many cases, through an effective cysto-aerogram obtained with little manipulation and no trauma. The roentgenograms obtained show greater contrast and clarify the bladder pathology. The vesical end of the ureters is better visualized.



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# ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

#### ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

WORTH, H. M. The use of lipiodol in the localisation of spinal tumours. *Brit. J. Radiol.*, April, 1938, 11, 211–226.

The general gross anatomy of the spinal cord and coverings is reviewed. The principal methods of injection are via the cisterna magna or by the lumbar route. Certain advantages and disadvantages claimed for both methods are summarized. Certain neurologists claim that the injection of lipiodol into the spinal canal is dangerous and harmful. The author has not been able to find any records of a fatal result. Elsberg found recent adhesions at operation after lipiodol injection.

Doses up to 5 cc. are necessary in order to recognize small changes. If a lumbar puncture with removal of fluid has been carried out very recently a relatively dry subarachnoid space prevents the free movement of the lipidol. The patient is placed and fixed in the supine position, and the lipiodol is studied on the fluorescent screen. The mass must be kept intact if possible. In the event of any suspicious appearance roentgenograms are taken at once. In many people there is a tendency for the lipiodol to become arrested at the site of the vertebral curves. In variations from the normal the lipiodol may become completely blocked, partially blocked, divided into two streams, or the mass may present a defect at its side, sides, or in its center. In cases of intramedullary tumors there is a tendency for the lipiodol to be displaced to the sides of the canal, forming two columns. However, intramedullary expansion of the cord may not produce a block of this type. Extramedullary intradural tumors which produce obstruction may reveal "cup-shape" indentation in the border of the arrested lipiodol. However, an extramedullary tumor may produce a block without the characteristic appearance. Small globules may be separated from the mass. This may not be of pathological significance but the arrest of a number of globules has been reported in arachnoiditis.

This article has a number of very good illustrations.—S. G. Henderson.

Lob, A. Das Röntgenbild und seine pathologisch-anatomischen Unterlagen bei der Ausheilung von Wirbelsäulenverletzungen. (The pathological-anatomical basis for the roentgen appearance in the healing of vertebral injuries.) Fortschr. a. d. Geb. d. Röntgenstrahlen, Sept., 1939, 60, 199–213.

While much is known about the healing of fractures of the long bones, there are many unsolved problems relating to fractures of the vertebrae. Vertebral fractures have been much more common because of heightened activity in industry, transportation, and sport, particularly skiing. The differences of opinion which exist concerning the treatment of such fractures further indicates the necessity for a better understanding of the healing process. The author, on the basis of pathological specimens, recognizes two types of injury: (1) the simple vertebral body fracture with no involvement of the arch, the processes, or the discs; (2) vertebral body fractures complicated by injuries of these other structures.

Simple fractures lead to the familiar wedge-shaped vertebra with a zone of disordered spongiosal bone usually parallel to the upper or lower border. There may be some angulation of the anterior border with folding of the anterior longitudinal ligament. After the injury the osteoclasts remove the disordered bone and simultaneously an osteogenic cell layer forms and leads to endosteal callus in the course of a number of months. Very little callus forms subperiosteally and often no change is demonstrable at the margins of the vertebra.

The complicated fracture shows involvement of the superior or inferior plates of the body and there may be avulsion of a fragment from one of the anterior angles as viewed in the lateral plane. In injuries of this type the interverte-

bral disc is always involved and tears may extend into the nucleus pulposus. Associated fractures almost always occur in the pedicles and the fracture line usually runs obliquely. It is recognized much more commonly in the pathological-anatomical preparation than in the roentgen films and may be accompanied by injury to the spinous processes. If the fracture occurs near the articular surface of the pedicle, healing may result in solid bone ankylosis at the involved joint. The fragments avulsed from the vertebral body unite with very little callus formation and over a long period the contour becomes smooth and rounded. Portions of the intervertebral disc which penetrate the fracture site become fibrous, but rarely ossify. If the annulus fibrosus is injured, spicule, beak and lipping formations occur at the margins of the vertebral bodies as the result of enchondral ossification in a cartilaginous overgrowth. This occurs in the course of two to three months after the injury and may result in laminated new bone with normal bone marrow. Injuries of this type are almost always accompanied by tears of the supra- and interspinal and interarcuate ligaments. The anterior and posterior longitudinal ligaments generally withstand the injury. In the dorsal spine the ligaments about the costovertebral joints may also be torn and there is usually hemorrhagic infiltration of the surrounding soft tissues over a large area.

The overgrowth which occurs at the margins of the vertebral bodies following trauma is an expression of injury to the intervertebral disc just as it is in primary spondylosis deformans. Such formations do not occur at the site of a vertebral injury unless there has been an accompanying injury to the disc. They cannot properly be regarded as "periosteal callus." True callus is sometimes recognizable; it is limited in extent and duration and occurs at the fracture site.

In estimating the healing of vertebral body fractures, one must remember that the fracture is only a part of the injury and that great consideration must also be given to the ligamentous injuries which occur about the joints.—
W. A. Evans, Jr.

TAYLOR, RAYMOND G. Anomalies of the lumbosacral articulations. J. Am. M. Ass., Aug. 5, 1939, 113, 463-465.

The fifth lumbar vertebra shows more anomalies than any other vertebra in the body. The commonest ones have to do with the

transverse processes and the articulations. The transverse processes may be short, almost rudimentary, long and slender, or broad and massive. The transverse process and the whole lateral mass may articulate with or may be actually fused with the sacrum. The articular facets are normally crescentic and the superior pair is slightly hollowed out and cuplike, the surface of the inferior facets being slightly convex to fit into the concavity of the facets of the vertebra below; normally they face laterally and slightly obliquely. The superior pair of joints of the fifth are generally of this type, but the inferior pair that articulate with the sacrum show wide variation in the direction the joint faces. Two main variations are relatively frequent. Each pair may face directly anteroposteriorly. A second variation shows the joint faces resting directly one above the other, facing in a caudad-cephalad direction. There may be a combination of any of these three types of joints. If one does not see through these joints in the routine type of anteroposterior roentgenogram they are abnormal as to their facing and the wider the articular process shows in the roentgenogram the more nearly the joints face anteroposteriorly. To see through these joints and to learn something of their condition, lateral and oblique views must be made.

Abnormal motion in these joints may result in damage to the joint or ligaments. With relaxed muscles and sudden unexpected strain, enough movement is possible either to damage the synovia or to strain the ligaments. Repeated damage to the same structure may sooner or later produce fibrous changes, scar tissue and in many instances calcium deposit in the injured tissues.

A consideration of extracts from some of the articles in the American literature shows that anomalies of the joints are common, that they give improper support to the body structures and are deficient in their weight-bearing and strain-resisting properties, and that the defects or anomalies allow damage to the joints and to their soft tissue supports, thereby being a fairly common and important cause of pain. It is obvious that most persons who have backs showing these anomalies are rather unsuited to hard manual labor as lifting and straining. They are more liable to injury than others with normal articular facets. Roentgenologic reports should call attention to these conditions.—S. G. Henderson.

McKeever, Francis M. Tuberculosis of the knee in infancy and childhood. J. Am. M. Ass., Sept. 30, 1939, 113, 1293–1299.

Author's Summary. For forty-seven patients in the first ten years of life suffering from proved tuberculosis of the knee joint, the most frequent age of onset was found to be within the first four years.

Fifteen patients, or 31.9 per cent, presented. a bone abscess in the metaphysial or epiphysial region of the tibia or the femur early in the disease.

One patient remained well, with a normal knee joint, for eight years after extra-articular excochleation of an osseous focus. In five other patients this procedure failed.

Conservative treatment, or surgical procedures short of economical resection, accomplished no satisfactory results in the remaining forty-six patients.

Economical resection healed the tuberculosis in thirty-two of thirty-four patients, or 94.1 per cent, whom it was possible to follow for from one and a half to thirteen years.

The knee joint of a child ankyloses very readily after resection, and the percentage of successful fusions resulting from a single operation is as high as that for ankylosing operations on any other joint.

Extreme shortening after economical resection in infancy and childhood is not the rule; any marked degree occurred in only 30 per cent of the patients. In these it usually resulted from causes extraneous to the resection.

Severe aberrations of directional growth were associated in most instances with previous damage to the epiphyses. They occurred in only  $33\frac{1}{3}$  per cent of the patients. Moreover, in these they were readily correctable by osteotomy.

From the evidence it seems reasonable to conclude that economical resection of the knee is not contraindicated prior to epiphysial closure, and this procedure should not be withheld until the age of 15 from children suffering from tuberculosis of the knee joint.—S. G. Henderson.

MEYERDING, HENRY W., and POLLOCK, GEORGE A. March fracture. Surg., Gynec. & Obst., August, 1938, 67, 234-242.

The authors discuss the various clinical features of so-called "march fracture," with special emphasis upon the predisposing and

exciting factors and the differential diagnosis. The roentgen evidence may be absent even though the diagnosis is strongly suggested clinically. The hair line fracture in the metatarsal bones may be visible only after repeated search. Later the fracture line may become easily visible after the subperiosteal new bone proliferation has supervened. Ten representative cases are reported. The condition may be confused with sarcoma and in all doubtful cases a biopsy should be done.—*P. C. Swenson*.

McReynolds, I. S. Osteolytic osteogenic sarcoma with a report of eight five-year survivals. Surg., Gynec. & Obst., August, 1938, 67, 163–168.

After discussing the gross and microscopic features of osteolytic osteogenic sarcoma as well as its tissue origin, the author reports on 8 five-year survivals. All were amputation cases and several had had one or more operative procedures to the tumor area prior to amputation. In a series of 131 cases studied from the Surgical and Pathological Laboratories of the Johns Hopkins Hospital, 47 per cent were in the second decade of life, 16 per cent in the third, and 8.5 per cent in the next three decades. Only I case was under the age of ten and 7 were over the age of sixty. Osteolytic sarcoma represented 24.1 per cent of all types of osteogenic sarcoma. Of 99 cases followed over a period of five years, 8 were alive; and 5 of the 8 lived approximately ten years or longer. Three died of metastases at six, seven and seven and a quarter years. In all, 92 per cent died from the effects of the disease prior to five years and 94 per cent died within eight years.

The author believes that osteolytic sarcoma may arise from benign giant cell tumor. The microscopic examination of these cases does not suggest that they are any less malignant but the several local operative procedures done in these cases probably would. The author cites one interesting case of metastases occurring seven years after amputation. In another the patient developed metastases three years prior to death which occurred five years after amputation. The metastatic lesions were kept under control by deep roentgen therapy. This is an unusually good palliation and suggests to the author that roentgen therapy should be given a trial in cases of pulmonary metastases. No change in the management of the treatment is suggested.

Perhaps the most important observation made in this study was that five-year survivals are less likely the younger the patient and the shorter the duration of symptoms.—P. C. Swenson.

#### BLOOD AND LYMPH SYSTEM

Häussler, Georg. Über die Darstellung der Hirngefässe mit Äthyltrijodstearat. (The demonstration of the cerebral vessels with ethyltrijodostearate.) Fortschr. a. d. Geb. d. Röntgenstrahlen, August, 1939, 60, 171–173.

The use of this finely dispersed colloidal substance in the demonstration of the liver and spleen has been recently reported by Beckermann. It is superior to thorotrast in not being radioactive and in being completely excreted by the body in a few days. Excellent results were obtained in visualizing the vessels of the brain upon injection of a 20 per cent solution and no evidence of damage was encountered.—
W. A. Evans, Jr.

HÄMMERLI, FORTUNAT. Über die Extremitätenarteriographie mit Äthyltrijodstearat. (Arteriography of the extremities with ethyltrijodstearate.) Fortschr. a. d. Geb. d. Röntgenstrahlen, August, 1939, 60, 173–175.

Arterial injection of this substance is painless, but produces a sensation of increased heat in the extremity, and a rise of 2° C. may be detected in the extremity for two days.

For arteriography it is recommended that the exposed artery be injected under local anesthesia with 8–14 cc. of the warm 20 per cent iodine containing sol.—W. A. Evans, Jr.

VEAL, JAMES Ross. The pathologic basis for swelling of the arm following radical amputation of the breast. Surg., Gynec. & Obst., Dec., 1938, 67, 752–760.

Venographic studies and local venous pressure determinations can be used in ascertaining the rôle of venous obstruction as a causative factor in the production of edema following radical amputation of the breast. The author describes three types of postoperative edema: (1) The lymphatic edema, least common (10 per cent) of cases, due to blockage of both the superficial and the deep lymphatics usually by early postoperative infection or a recurrent lymphangitis or cellulitis of the arm and shoulder, but less often due to direct extension of carcinoma into the skin and subcutaneous tissues of the arm. The venogram shows no ob-

struction. (2) Edema due to venous obstruction of the soft pitting variety as contrasted to the brawny lymphatic type (most common—90 per cent of cases) caused by the pressure of the continuously spreading new growth or by its constricting action. New growth may invade the lumen directly and plug it by tumor mass or by secondary thrombosis. Scarring may also be a factor. Venographic studies show the occlusion of the axillary vein and demonstrate the development of new venous channels. Venous pressure determinations are of value if the obstruction cannot be visualized because it lies proximal to the entrance of the external jugular into the subclavian vein. Pressures are recorded from 19.5 to 140 mm. of water in the edematous arm. (3) Edema from lymphaticovenous obstruction, an advanced form of the second type leading into a combination of the first two. Infection is prone to occur in this type which further increases the lymph stasis. —P. C. Swenson.

#### GENERAL

Hellman, Louis M., and Irving, Frederick C. The x-ray diagnosis of erythroblastosis. Surg., Gynec. & Obst., Sept., 1938, 67, 296–298.

The authors present 3 cases of erythroblastosis of the hydrops variety in which the diagnosis was established (by means of the roentgen ray) prior to the birth of the infant. Because this type of erythroblastosis is incompatible with life, and because there is a 30 per cent familial incidence of the disease with 50 to 80 per cent chance of recurrence in the same family, the prenatal diagnosis is of more than academic interest. The diagnosis depends on the presence of an advanced edema of the soft parts which the authors say can be recognized in the roentgenogram as a thickening and increase in density of the soft parts, particularly striking in the scalp. This edema is not necessarily limited to this disease, however, so that the roentgen findings are not specific. It is unfortunate that the reproductions of the authors' roentgenograms are not very convincing.-P. C. Swenson.

#### ROENTGEN AND RADIUM THERAPY

GILBERT, RENÉ. Die Entwicklung der Strahlentherapie einiger generalisierter. Erkrankungen im Laufe der letzten 10 Jahre. (The development of radiation therapy of some

generalized diseases during the last ten years.) Strahlentherapie, 1938, 63, 385-392.

In this work the author considers radiation therapy in chronic leukemia, essential ervthremia and in lymphogranuloma. Up to 1927, with the exception of animal experiments only so-called local segment irradiations of the human body were carried out. This type of procedure was classical irrespective of whether one had to deal with a local or a generalized affection. It has been known for a long time that leukemia and lymphogranulomatosis are radiosensitive. With the improvement of technique these two diseases began to be treated more successfully by the roentgen ray. At this time an attempt was made to irradiate the entire body. It was found that under this method of treatment in combination with arsenic medication, it was possible to prevent the appearance of a growing resistance to . roentgen radiation. This statement was at first made by Naegeli and was later confirmed by Schinz and others. Naegeli is of the opinion that at first the individual suffering from leukemia should be treated intensively by oral and parenteral arsenic therapy. The results of the treatment must be judged by the condition of the blood picture as a whole and not by the number of leukocytes only. This form of roentgen treatment of leukemia is preferable to the old classical form, since the clinical results obtained by it are considerably superior and since to a certain extent the possibility of development of resistance to the roentgen ray is eliminated. Using this method of treatment good results were supposedly obtained by Cottenot and Sluys in cases of lymphatic leukemia.

In cases of erythremia or Vaquez's disease, Sgalitzer reported in 1937 to have obtained favorable results in 42 of the 44 cases treated by him roentgenologically. The results are very encouraging but just as in leukemia no cure is obtained. Using the generalized roentgen method of treatment, it is possible to lower the red cell count to 4,000,000 at a time when the white cell count does not decrease below 3,000.

In lymphogranulomatosis or Hodgkin's disease, the effect of the generalized roentgen treatment is different than in the other two diseases mentioned. Here it leads to severe general symptoms and consequently some authors prefer here roentgen treatment of the entire trunk of the body with large individual fields combined with local irradiations of the

the indication for irradiation must be based on an evaluation of the entire blood picture. In cases where the blood picture is of a nature which indicates the desirability of roentgen irradiation, a pure qualitative blood picture as a whole must not serve as a contraindication to irradiation. The presence of a large number of immature cells is no contraindication to roentgen irradiation if one is not dealing with the terminal stage of the disease. Even an extremely poor function of the erythropoiesis is no contraindication to roentgen therapy since the poor erythropoiesis may be due chiefly to an injury of the blood forming organs by the leukocytic hyperplasia. In cases of this type roentgen therapy is actually followed by an increase of the red cell count, proving, therefore, the degree of effectiveness of the therapy. In cases, however, where roentgen therapy is followed by a further increase of the anemia, this response points to irreparable destruction of the erythropoietic tissue and further roentgen therapy is useless.

During irradiation an attempt must be made not to obtain a very rapid destruction of the leukocytes. Every second day a thorough study of the blood must be carried out during the irradiation. The irradiation technique must, therefore, also prevent a rapid destruction of the leukocytes. Considerable attention must be paid also to the behavior of the lymphocytes. A rapid decrease in the number of lymphocytes in association with a high leukocyte count is a dangerous sign and in each case where the lymphocyte count decreases to 2,000 the irradiation must be discontinued. In cases where irradiation is followed by a decrease in the number of red cells, by a decrease in the hemoglobin, and by an increase of the reticulocytes, irradiation must also be discontinued.

In chronic lymphadenoses attention may be called to two factors: The constant decrease of the thrombocytes is progressive with the progress of the disease. The hyperplastic lymphadenoid tissue in the glands and in the spleen requires large radiation doses which may be injurious to the radiosensitive cells of the myeloid series. A decrease of the absolute granulocytes up to 3,000 and a decrease of the thrombocytes to 100,000 necessitate a discontinuance of roentgen therapy in lymphatic leukemia.

Just as in the leukemic diseases, also many cases of lymphogranulomatosis may be favorably influenced by roentgen irradiation. Great care is necessary, however, in the choice of proper cases suitable for this treatment. In cases of acute lymphogranulomatosis combined with septic temperature, a leukopenia and a rapidly increasing anemia, radiation therapy is actually injurious. Of the other forms, especially the localized type is suitable for roentgen treatment. Also in lymphogranulomatosis, therefore, the radiation therapy must be carefully controlled and regulated by a thorough study of the blood.—A. S. Schwartzman.

Carrie, C. Zur Therapie der Röntgenstrahlenleukopenie (The treatment of roentgen-ray leukopenia.) *Strahlentherapie*, 1938, 63, 183– 187.

Feller recently reported, on the basis of experimental studies, that the effect of radium on the blood picture is similar to that of benzol, but that definite differences are present on the basis of which the two effects cannot be considered as fully identical. Friemann was able to confirm the occurrence of leukopenia following benzol intoxication in individuals employed in certain industries and later he was able to obtain experimentally the leukopenia in animals. Friemann later found that the experimentally produced benzol leukopenia in animals may be eliminated or prevented by the administration of vitamin C. In consideration of these findings an attempt was made by this author to determine the effect of vitamin C on roentgen-ray leukopenia.

It has been found that roentgen irradiation is followed by a definite decrease of the white cell count, especially when the irradiations have to be given at short intervals of time in the course of a long period, for instance, in cases of treatment of malignant tumors. The use of vitamin C by this author revealed that the roentgen leukopenia can be favorably influenced by it. It is conceivable that during the roentgen irradiation the normal vitamin C content is decreased and that the additional administration has a favorable effect on the leukopenia. Especially good results are obtained when the vitamin C administration is instituted at the same time as the roentgen treatment. It is desirable, therefore, to begin the vitamin C administration simultaneously with the roentgen irradiation. The impression was also obtained that roentgen irradiation was better tolerated by all the patients who received the vitamin C.—A. S. Schwartzman.

LÜSEBRINK, HANS. Veränderungen des weissen Blutbildes nach Grenzstrahlenbehandlung Lupuskranker. (Changes in the white blood picture following treatment of lupus with grenz rays.) Strahlentherapie, 1938, 63, 77–81.

In the literature a number of changes in the white blood picture following treatment of the skin with grenz rays have been reported. In most of the cases these changes were observed a limited length of time following the irradiation. In some instances the blood picture was studied from a few minutes up to twelve to twenty-four hours following the irradiation. Leukocyte variations up to 2,000 per cu. mm. have been described. In studies of this type the physiologic daily rhythmic variations in the blood picture must be considered. Sabin and her coworkers have observed variations in the leukocyte count for which no demonstrable reason could be elicited, presumably occurring every fifteen minutes and of a considerable degree. In studying the effect of the grenz-ray irradiation one must, therefore, be extremely careful and must make absolutely sure that the variations are not physiologic but actually the result of the irradiation.

This author studied the blood picture of irradiated lupus patients at intervals of forty-eight hours and these studies were carried out in the course of four weeks. The blood was always obtained on an empty stomach at the same time of the day and under approximately the same environmental conditions. In about 50 per cent of the cases studied the lupus focus was superficial and was removed by means of an electric snare after which it was irradiated. In the remaining 50 per cent the lupus focus was irradiated only. The surface irradiated varied from 100 to 300 sq. cm. The dose employed was always 4,000 r. All the patients studied were on a salt poor diet.

At first the leukocyte count was obtained daily on 15 patients. In 14 cases the following day after the irradiation there was observed a

decrease in the leukocyte count but this was not comparable with the decrease of the leukocyte number reported in the literature presumably observed under similar circumstances. In only one case could a decrease in the leukocyte count not be observed in the days following the irradiation. In 2 cases the leukocyte count was somewhat increased twenty-four hours after irradiation but during the following days it definitely decreased. The maximum leukocyte count obtained in these cases varied between ten and eleven thousand.

Besides the leukocyte count a differential count was also carried out. A definite variation could be observed only in the leukocytes and in the eosinophiles. No difference was found in the cases where the focus was previously removed and then irradiated and in the cases where irradiation alone was carried out.

In 13 of the 15 cases studied the number of the lymphocytes increased reaching the maximum in four to six days after which it returned to normal in a few days, and reaching another maximum fifteen to twenty days after the irradiation. The second maximum was not as pronounced as the first.

Two maxima were also found in the eosinophiles, the first appearing on the sixth to the eighth day and the second on the fifteenth to twentieth day after the irradiation.

In each case the blood sedimentation rate of the red cells was studied but apparently no demonstrable influence on the irradiation was observed.

Nothing definite can be stated as to the reason for this variation in the white blood cells. In all probability one is dealing here with an absorption of specific substances from the lupus foci conditioned by the influence of the rays; it is also conceivable that the vegetative nervous system may originate these variations. Further comparative studies on healthy and tuberculous skin may elicit the nature of these changes.—A. S. Schwartzman.



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#### MALIGNANT TUMORS OF THE KIDNEY IN ADULTS\*

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THIS paper is based on the analysis of 50 cases of malignant tumors of the kidney in adults. Only cases that have been verified by the microscopic study of tissue removed either at operation or necropsy are included.

A great deal of controversy and confusion exists in the pathologic classification of these tumors. However, from the standpoint of clinical and roentgen diagnosis, they fall into two main groups. First, those arising from the kidney pelvis, which may be either papillary or sessile; and secondly, those arising within the kidney, the so-called "hypernephroma" or renal cell carcinoma. No attempt will be made here to classify them further.

### MALIGNANT TUMORS OF THE KIDNEY PELVIS

Five of the 50 patients had tumors arising within the kidney pelvis. The involvement was on the right 3 times, and on the left twice. All these tumors were of the papillary type. Three patients were men, and 2 were women. One patient was thirty-four years of age, and 4 were over seventy.

Hematuria was the first symptom in each case. It was intermittent in character,

and had been present from six months to five years before the patient was first seen. Blood clots were passed at some time by each patient. All 5 cases had a moderate secondary anemia, the average red blood cell count being 3,250,000 in the men, and 3,865,000 in the women.

One patient complained of a dull, aching pain in the flank, and 2 had colic accompanying the passage of blood clots. A palpable tumor was present in only one patient.

Kidney stones were found once, and these were in the only patient giving a history of having passed calculi. Secondary tumor implants into the bladder were found in 3 of these patients.

Roentgenograms were made on all 5 patients. While this small number is insufficient to be conclusive, it is observed that on retrograde pyelograms a small papillary tumor produces an irregular filling defect without distortion of the uninvolved portion of the pelvis, and with no distortion of the kidney outline (Fig. 1). Whether such a tumor is benign or malignant cannot be determined from the roentgenogram. While blood clots do produce defects, they tend to be smooth in outline rather than irregular as occurs with a papillary tumor.

<sup>\*</sup> Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19-22, 1939.



Fig. 1. Small papillary tumor of the kidney pelvis showing an irregular filling defect, but without distortion of the uninvolved portion of the kidney pelvis or of the kidney outline.

They also can usually be ruled out by repeated washing of the kidney pelvis.

With larger papillary tumors, the pelvis may be almost completely filled with neoplastic tissue. Tumors of this size distort the kidney pelvis and may obstruct some of the calyces with resultant localized hydronephrosis. Even though the kidney pelvis is nearly filled with tumor tissue, the outline of the kidney remains intact, providing there has not been marked invasion of the parenchyma (Fig. 2).

Tumors of the kidney pelvis may, however, invade the kidney to such an extent that there is distortion of the kidney outline and a mass becomes palpable. In this event, it may be impossible to differentiate between such a tumor and a primary tumor of the kidney secondarily invading the pelvis. In one of our cases, the ureter was found to be completely occluded by tumor tissue so that a satisfactory pyelogram could not be obtained.

Because of the high incidence of bladder implants (3 out of 5 in this series), it would seem advisable to make cystographic studies on all patients suspected of having tumors of the kidney pelvis. These secondary tumors are readily visualized on air cystograms (Fig. 3), or with opaque cystograms when the tumor is observed in profile or through a not too dense medium.

## $\begin{array}{c} \text{MALIGNANT TUMORS ARISING WITHIN} \\ \text{THE KIDNEY} \end{array}$

Forty-five of the 50 patients had tumors arising within the kidney. Thirty-three were men, and 12 were women—a ratio of nearly three to one. The patients' ages

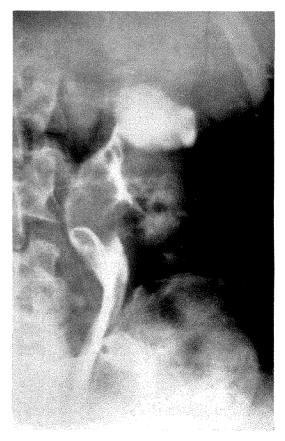


Fig. 2. Papillary tumor nearly filling the kidney pelvis and producing a localized hydronephrosis in the upper pole. There is no distortion of the kidney outline.

varied from thirty-three to seventy-six, the average being fifty-seven years and eight months. Two-thirds were in the fifth and sixth decades.

Hematuria was the first symptom noticed by 24 patients, although it was present at some time, but was not the first symptom, in 10 additional cases.

The hematuria was intermittent in character lasting usually from one to three days, and then disappearing for a variable period of time. Twenty-four patients gave a definite history of passing blood clots. Thirteen of these stated that they had at some time passed clots, worm-like in shape, indicating that the clots had come down the ureter.

Nearly every patient had a moderate secondary anemia. The lowest red blood cell count was 2,100,000. The average for

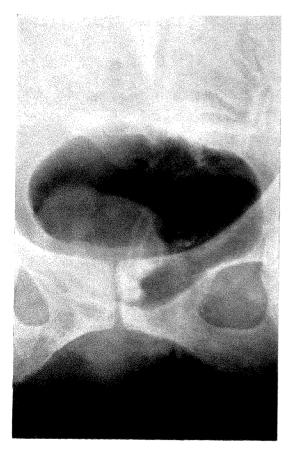


Fig. 3. Air cystogram demonstrating a large secondary implant in the bladder wall from a primary papillary tumor of the kidney pelvis.

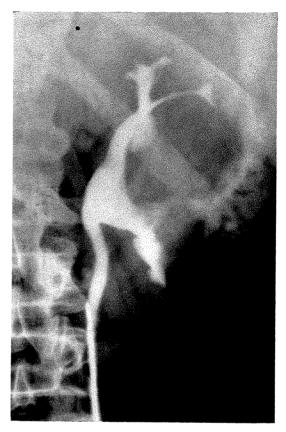


Fig. 4. Kidney tumor showing typical elongation and compression of upper and middle calyces.

men was 4,036,000, and for women 3,765,-000.

Pain was the first symptom in 6, although it was present at some time in 24 others.

The pain complained of was of two types. First, a dull "aching", "dragging sensation", or "feeling of discomfort" in the flank noted by 17 patients. This was apparently due to streching of the kidney capsule or the weight of the tumor mass, since a palpable tumor was noted in 15 of these 17 patients. Secondly, a "sharp, colicky" pain accompanying the passage of blood clots and stressed by 13 patients. Stones were not found in any case, and only one patient gave a history of having passed calculi previously.

Tumor was the first symptom noticed by 6 of the patients. On physical examination, a tumor was palpable in 32 patients.

Loss of weight and weakness was the



Fig. 5. Large kidney tumor demonstrating elongation, narrowing, and wide separation of the major calyces.

chief complaint in 4. However, a history of loss of weight was obtained in 21 patients. In 17 of these the amount was stated and this averaged 46 pounds and took place over an average period of nine months. Twenty patients gave no history of weight loss, and in 4 no mention of weight was made in the record.

In only 2 were the first symptoms due to metastasis. One patient complained of a persistent cough and was found to have extensive lung metastasis at necropsy. The second patient developed personality changes from brain metastasis and was first committed to the psychopathic ward.

In 3 patients there were no symptoms referable to the kidney, and the tumor unsuspected during life was found at necropsy.

The duration of symptoms varied great-

ly. Two patients gave a history of intermittent hematuria going back over a period of fifteen years, a third for ten years, and a fourth for nine years.

Whether maligant kidney tumors can be present and produce symptoms for such a long period of time or whether the hematuria was coincidental to some unrelated cause is open to speculation. However, one patient, in whom the kidney was found to be replaced by tumor tissue at necropsy, was known to have had a palpable mass on the involved side for eleven years. A gland showing metastasis was also removed from his neck four years before death.

As previously noted, 3 patients had no symptoms referable to the kidney. Others had symptoms for only a few days or weeks before entrance. In those patients on whom

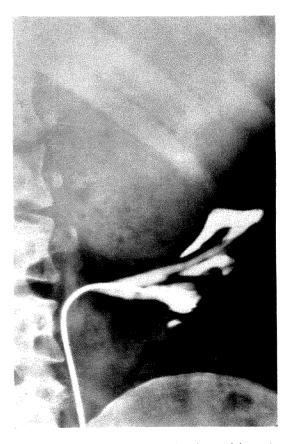


Fig. 6. Large kidney tumor showing calcium deposits. There is marked displacement of the kidney pelvis and calyces accompanied by elongation and narrowing of the calyces.

a history could be obtained, the average duration of symptoms before entrance to the hospital was twenty-five months.

The right kidney was involved 18 times, and the left 26. In one patient examined at necropsy, small, apparently primary tumors were found in the upper pole of each kidney. Of the remaining 44 patients, the upper pole was involved 15 times, the lower pole 17 and the middle or entire kidney 9 times. In 3 the location was not given in the record.

Fever has been mentioned in the past as sometimes being a remarkable concomitant symptom of renal tumors. Although specifically looked for in the records of this series, with possibly two or three excep-

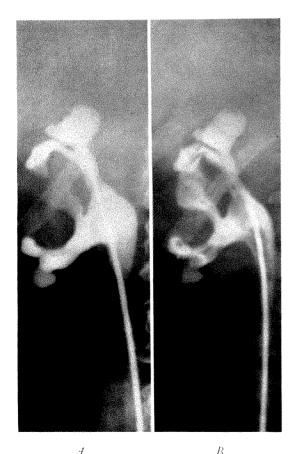


Fig. 7. A, tumor involving the central portion of the kidney. Pyelogram taken following washing out of blood clots from the pelvis. B, pyelogram taken before washing kidney pelvis and showing smooth filling defects due to clotted blood.

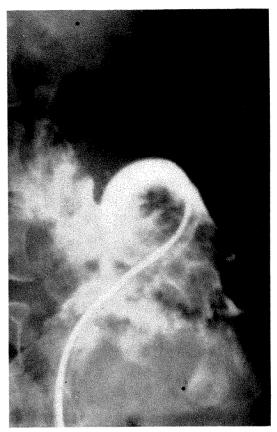


Fig. 8. Pyelogram demonstrating invasion of the kidney pelvis by tumor tissue with resulting loss of the normal outline of the pelvis and calvees.

tions, there were no patients with elevations of temperature that could not be accounted for by accompanying low-grade infection or reaction following cystoscopy. The majority of these patients, however, were under direct observation for only short periods of time.

The white blood cell counts were also for the most part within normal limits. Except for one patient with leukemia, the highest count was 23,000; only 5 were over 15,000; and the average was 9,400.

Flat films of the urinary tract and stereoscopic anteroposterior retrograde pyelograms were obtained on 34 of these patients. Additional lateral pyelograms were made in a few instances. The flat films frequently showed important positive diagnostic information such as increase in size

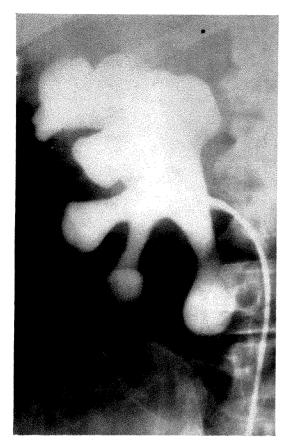


Fig. 9. Rarely seen deformity of kidney tumor in which there is dilatation of the kidney pelvis and calyces, but with elongation of the major calyces.

or density of the kidney, irregularity of outline, or the presence of calcium deposits.

Areas of calcification subsequently shown to be within kidney tumors were discernible on the films of 13 of the 34 patients roentgenographed. These deposits usually appeared as diffuse amorphous flecks although occasionally there were accompanying irregular plaques. Calcification was present in small tumors and appeared to bear no relationship to the size of the neoplasm.

In retrograde pyelograms, the most constant and characteristic finding was elongation and compression of one or more of the major calyces. This type of deformity was present in 23 of the 34 pyelograms. It occurs with both small and large tumors, and takes several forms. Only one or two

calyces may be involved (Fig. 4), or all calyces may be elongated, compressed, and widely separated producing the so-called "spider-leg" deformity (Fig. 5). In other instances, the pelvis and calyces may be pushed to one side, but still with elongation and compression of the major calyces (Fig. 6). These changes are sometimes better demonstrated in a lateral view.

From roentgenographic observation, invasion of the kidney pelvis by tumor tissue is not a frequent occurrence. Blood clots, when present, produce filling defects which are smooth in outline and of uniform negative density (Fig. 7).

Less commonly (8 cases) there was more or less complete obliteration of the usual landmarks of the pelvis and calyces. Injected opaque material was diffused into a conglomerate mass of tumor tissue and blood clots, and produced a pyelogram characterized by the absence of any form or shape (Fig. 8).

Rarely (3 cases) the pyelogram showed marked enlargement and dilatation of the kidney pelvis and calyces, with elongation of the major calyces, but with little or no compression (Fig. 9.).

In all pyelograms, as well as on plain films, abnormalities in kidney size, contour and density should be specifically looked for.

In retrospect, in no instance was a pyelogram obtained that could be considered normal, although admittedly an elongated upper calyx from a tumor resembles a normal bifid type of kidney pelvis.

#### SUMMARY

Fifty cases of verified malignant tumors of the kidney in adults have been studied.

Tumors primary in the kidney pelvis were found in 10 per cent of the cases. In this group intermittent hematuria was the first symptom in each case. Accompanying stones were present only once.

There is no apparent predilection for side of involvement or sex of the patient. Secondary implants to the bladder occurred in 60 per cent of the cases. With small and moderate sized tumors, pyelograms show irregular filling defects without distortion of the kidney outline.

Large tumors invading the kidney cannot be distinguished from primary kidney tumors invading the kidney pelvis.

Malignant tumors, primary in the kidney, were present in 90 per cent of the cases of this series. These occurred in men nearly three times as frequently as in women. The average age of these patients was fifty-seven years and eight months with two-thirds of them being in the sixth and seventh decades.

The first symptom complained of varied in different patients. Hematuria was noted by 53 per cent, pain by 13 per cent, tumor by 13 per cent, loss of weight and weakness by 9 per cent, symptoms due to metastasis by 4.5 per cent, no symptoms by 7 per cent. However, during the course of their illness most patients had more

than one symptom so that hematuria was mentioned by 75 per cent, blood clots by 53 per cent, pain by 67 per cent, loss of weight by 47 per cent, and tumor was felt in 71 per cent of the patients.

The right kidney was involved in 41 per cent of the cases, and the left in 59 per cent.

In plain roentgenograms, changes in size, shape and density of the kidney, as well as calcium deposits which occurred in 38 per cent of the roentgenographed cases, should be looked for.

Retrograde pyelograms, in the presence of tumor, show most frequently elongation and compression of one or more of the major calyces. Less commonly, there may be complete loss of the normal pelvic landmarks; and rarely, dilatation of the pelvis accompanied by elongation and dilatation of the calyces without remarkable compression.\*

\* For discussion see page 657.



#### ANOMALIES OF THE URINARY TRACT\*

By WILLIAM J. BAKER, M.D. chicago, Illinois

MUCH praise must be given to the roentgenologists for their aid to the urologists in making the diagnosis of anomalies of the urinary tract a common occurrence. It is estimated that over 40 per cent of renal and ureteral pathology, usually due to poor drainage and sepsis, occurs in the presence of anomalies of these organs. This fact makes a knowledge of the anomalous possibilities of the greatest importance.

In Figure 1, it is seen that the ureterorenal bud arises on either side from the wolffian duct, near the junction of this duct with the primitive cloaca; this begins about the fourth week of embryonic life. This epithelial bud from the wolffian duct produces the ureter, renal pelvis, calyces, papillary ducts and collecting tubules; the kidney mass of cells produces the convoluted tubules, the loops of Henle, Bowman's capsules and the glomeruli. Any change in or interference with the ureteral bud or kidney blastema probably causes anomalous conditions; these changes are excessive or arrested development or are the result of fission or fusion. It is said that the tubules of the renal mass may make improper connections with the glomeruli above or the minor calvees below and remain as potential cysts through excess exudation. It is not difficult to visualize two separate ureteral buds on one or both

sides to make ureteral duplication; or a fission of one ureter to make partial ureteral duplication or a double renal pelvis; or a fusion of the lower or upper poles of the kidneys to produce all kinds of fused kidneys. A great many anomalies of position undoubtedly develop when the kidney migrates from its pelvic to its permanent lumbar position; this adult kidney position is usually reached by the end of the ninth week of embryonic life. Whether dystopia is due to persistent transient blood vessels which prevent ascent of the kidneys is still debatable. Other anomalies of position are due to faulty rotation of the kidney around its longitudinal axis; the primitive pelves are originally situated ventrally and rotate to face laterally.

I. The most important anomaly of number is the absence of one kidney to produce a solitary kidney. Its importance lies in the fact that solitary kidneys have been removed due to trauma or acute pathology; uremic deaths have followed in ten to twenty-seven days. Figure 2 shows a ureteral stone which has passed down from a solitary kidney; cystoscopy revealed the absence of the right ureteral orifice and the right half of the trigone. In some of these patients there are normal ureteral orifices but one of them will end in a blind stump. Figure 3 demonstrates misinterpretation of intravenous urography in determining

\* From the Urological Services of Drs. Harry Culver and William J. Baker of St. Luke's and Cook County Hospitals, Chicago, Ill. Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

Legends for Figures 1-8, next page.

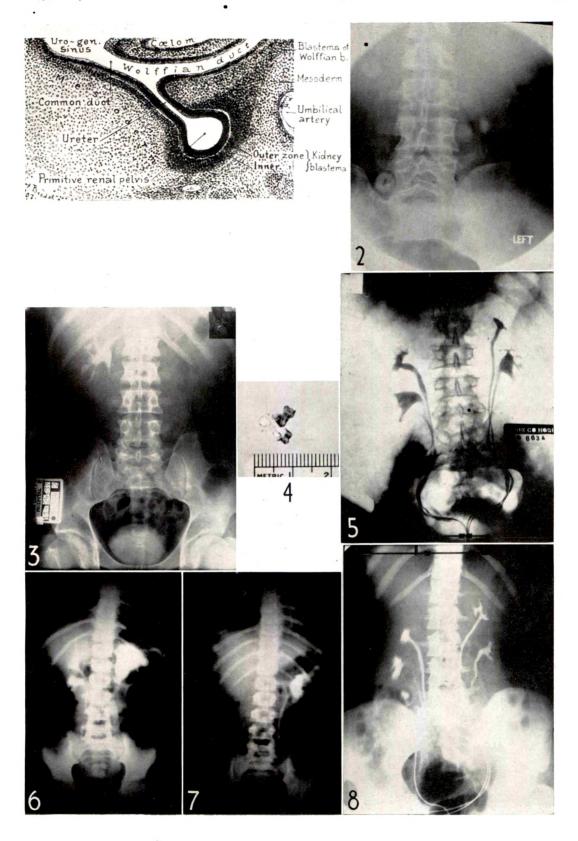
Fig. 1. Embryologic derivation of ureter and kidney.
Fig. 2. Ureteral calculus from solitary kidney.
Fig. 3. Solitary kidney; low left phlebolith which was mistaken for ureteral calculus.
Fig. 4. Phlebolith.

Fig. 5. Bilateral double kidneys and ureters.

Fig. 6. Infected hydronephrosis in upper half of left double kidney.

Fig. 7. Six month postoperative pyelogram after heminephrectomy of infected hydronephrosis (Fig. 6).

Fig. 8. Extrarenal shadow and bilateral double kidneys and ureters.



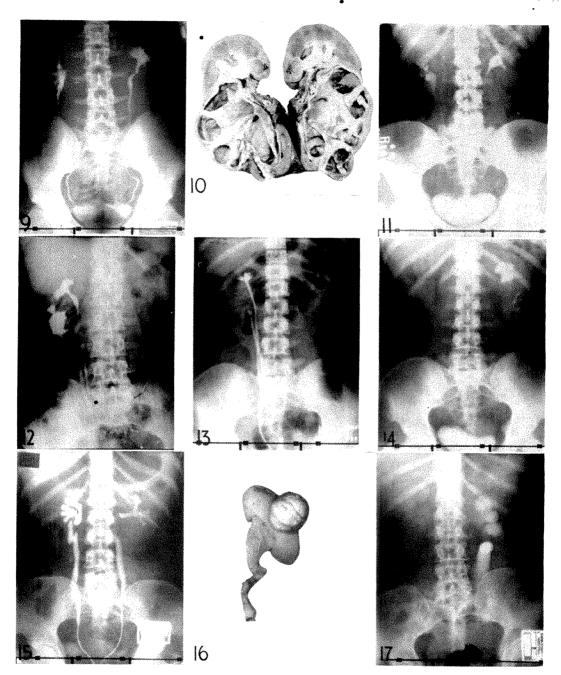


Fig. 9. Infected upper half of unilateral left double kidney.

Fig. 10. Kidney specimen of Figure 9.

Fig. 11. Unilateral right double kidney.

Fig. 12. Infected hydronephrosis of lower half of unilateral right double kidney.

Fig. 13. Calculus in lower half of right double kidney.

Fig. 14. Calculus in upper half of left double kidney.

Fig. 15. True hypoplastic infected right kidney.

Fig. 16. A renal cyst.

Fig. 17. Pyo-ureteronephrosis with no evidence of cyst in Figure 16.

the presence of both kidneys; a normal right kidney and ureter are shown; a shadow, similar to a low left ureteral stone, is seen in the region of the lower third of the left ureter; this stone was removed and proved to be a phlebolith as shown in Figure 4; later retrograde urological study proved the absence of the left kidney and ureter.

Double kidneys may occur on one or both sides. Figure 5 shows bilateral double kidneys in a female adult, who did not manifest pathology until late in life. Figure 6 shows bilateral double kidneys in an eight year old girl; the upper left kidney is an infected hydronephrosis. The upper half of double kidneys is usually the smaller of the two kidneys and the seat of more pronounced pathology. In order to be conservative, a left hemi-uretero-nephrectomy was performed and Figure 7 shows the six month postoperative pyelogram of the remaining left kidney. Figure 8 reveals bilateral double kidneys in a female adult who was subjected to urological study because of the extrarenal shadow on the right side. Figure 9 shows the upper half of a unilateral left double kidney in a boy, aged seventeen, who had had repeated left-sided colic as long as he could remember. Attention is drawn to the carnation type of pyelogram which usually indicates a double kidney. Note the constriction near the renal pelvis. This kidney was removed and the constriction was found to be caused by a moderate-sized aberrant vessel. Too many aberrant vessels prevented conservative heminephrectomy. Figure 10 is a photograph of the removed kidney. Figure II shows a unilateral right double kidney which was discovered when the patient was studied during a pyelitis of pregnancy. Figure 12 reveals a unilateral right double kidney in a male adult; the kidney was removed because of frequent recurrent attacks of pyelitis and an uncontrollable urinary tract infection. Figure 13 shows the right side of a bilateral double kidney of a female adult; a stone is seen in the pelvis of the lower right kidney; this kidney was

removed elsewhere in 1933 because of a calcareous pyonephrosis. She consulted us in January, 1939, and a stone was found in the upper half of her double left kidney (Fig. 14). A heminephrectomy was performed.

- 2. A surgically important anomaly of size is the true hypoplastic kidney; its symptoms are confusing because pain and discomfort often occur in the normal but greatly hypertrophied kidney which usually accompanies a true hypoplastic kidney. Figure 15 shows a true hypoplastic infected right kidney and a large normal left kidney; the hypoplastic kidney was removed.
- 3. Anomalies of form of the kidney are encountered frequently. A kidney may be made wider or longer by new growths or cysts. All sizable cysts of the kidneys are probably congenital. Many of them are symptomless and are discovered with other pathological lesions. Figure 16 shows a renal cyst which accompanied a pyo-ureteronephrosis due to a low ureteral stricture which followed radium treatment of the uterine cervix. The ureteropyelogram gave no indication of the presence of this cyst (Fig. 17). Many of these renal cysts produce anomalies of position as well as of form. Figure 18 reveals a left kidney which has been pushed far toward the midline by a very large cyst; the entire kidney and cyst were removed. Cyst formation or degeneration may be entirely unilateral and produce symptoms over a long period of time. Figure 19 shows the ureteropyelogram of such a cystic kidney which was removed. The polycystic kidney which undoubtedly has a congenital impetus, produces varied and bizarre anomalies of form, in addition to nephritic findings and occasional hypertension. Figure 20 is a pyelogram of a far advanced palpable polycystic kidney; the condition was bilateral. Figure 21 is a secretory urogram of a boy, aged eleven, with bilateral polycystic kidneys; his father, who is alive and feels well, has the same condition; his deceased paternal grandfather also had the same condition. Figure 22 shows this boy's

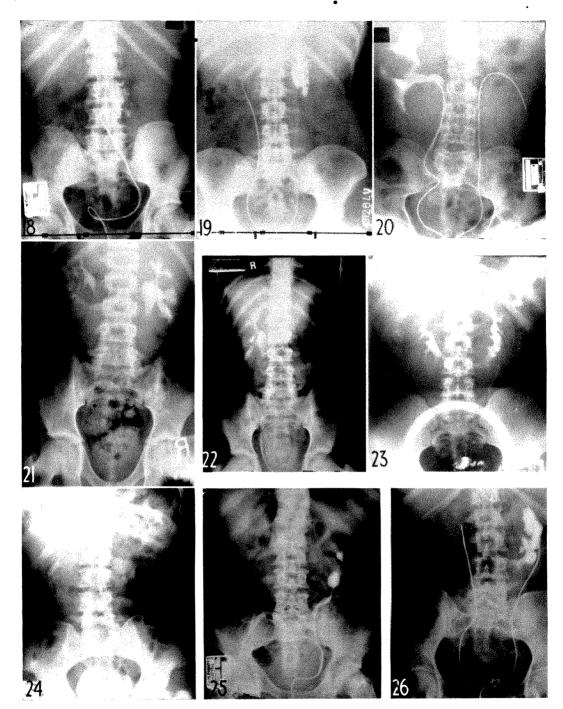


Fig. 18. Anomalous renal position due to a large renal cyst.

Fig. 19. Chronic cystic renal degeneration

Fig. 20. Right polycystic kidney.

Fig. 21. Bilateral polycystic kidneys in a boy, aged eleven.

Fig. 22. Right pyelogram of polycystic kidney of Figure 1, two years later.

Fig. 23. Normal horseshoe kidney.

Fig. 24. Low left ureteral stone and horseshoe kidney.

Fig. 25. Calculi in left half of fused kidney.

Fig. 26. Calculus in left half of fused kidney.

right pyelogram which was taken two years later.

The symmetrically fused or horseshoe kidney produces many anomalies of form: such a kidney may manifest itself by indefinite abdominal pains, chronic constipation and urinary disturbances but its anomalous blood supply and ureteral insertions cause poor drainage so that it may become infected or harbor calculi. The hila of these kidneys usually face ventrally and medially. Figure 23 shows a normal horseshoe kidney in a male, aged twenty-six, who was operated on because of epigastric and upper right abdominal quadrant pain; it was planned to resect the isthmus of the fused kidney and suspend the right half of the kidney. Surgical inspection revealed a very large distended gallbladder and a normal horseshoe kidney. The kidney incision was closed and the gall bladder was removed later. Figure 24 shows a low left ureteral stone and the presence of a horseshoe kidney; the stone was removed and recovery was complete. Figure 25 shows two stones in the left half of a fused kidney: these were removed by anterior pyelotomy. Figure 26 shows a stone in the left half of a fused kidney; note the high insertion of the ureter and the shadow cast by the isthmus which joins the two kidneys. Figure 27 reveals a staghorn calculus in the right half of a fused kidney; a left heminephrectomy was done with complete recovery. As a general rule, removal of either half of a horseshoe kidney is difficult because of the complex and anomalous blood supply.

4. Anomalies of position should be diagnosed with reticence. If a patient knows that he has a movable or floating kidney, it will be blamed for any and all of his symptoms; many movable kidneys produce no symptoms. To diagnose ptotic kidneys, urograms must be done in flat and upright positions. Figure 28 shows third degree renal ptosis and a marked ureteral kink in a female adult; she had much pain and a persistent bacilluria. Nephro-ureterolysis and nephropexy gave complete relief.

Figure 29A shows a movable kidney in a male adult •who suffered periodic severe renal or ureteral colic; operative interference afforded him complete relief. Extrarenal encroachments produce anomalies of renal and ureteral position which are sometimes confusing. Figure 29B is a urogram of a female adult; a diagnosis of renal tumor was made; surgery revealed a large aneurysm of the renal artery which had displaced the kidney and ureter. Aneurysms of the renal artery are notable for a lack of audible bruit or palpable thrill.

When the normal ascent of the kidney is interfered with, an ecotopic organ results. The left kidney is usually affected. Figure 30 reveals a stone shadow which was thought to be in the urinary bladder. A cystogram proved it to be extravesical. Further study located the calculus in a left ectopic kidney; the stone was removed through a transperitoneal pyelotomy. Figure 31 shows a symptom-producing left ectopic kidney in a male adult who had undergone three laparotomies before the cause of his symptoms was discovered. Figure 32 shows a left ectopic kidney which produced pelvic pain; this pain disappeared when the infection in the ectopic kidney was cured. Figure 33 illustrates a confusing picture of a left ectopic kidney in a female adult and a round opaque partially calcified body at its superior pole; bowel study and lateral roentgenograms indicated that this mass was attached to the kidney; it proved to be a large retroperitoneal lymph gland as shown in Figure 34. Figure 35 shows a left ectopic kidney in a male adult which was so painful that a nephrectomy was done. Occasionally one sees a bilateral fused ectopia as illustrated in Figure 36. This occurred in a female adult and non-interference was advised.

5. As the kidney rises from its pelvic to its permanent lumbar position it rotates partially around its longitudinal axis so that the calyces face laterally; incomplete or exaggerated phases of this rotation produce certain anomalies of location of the calyces, pelvis, ureter and blood vessels.

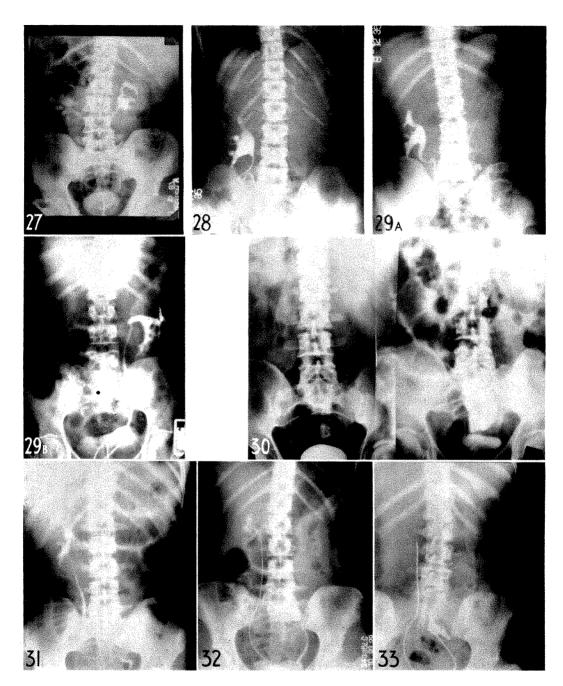


Fig. 27. Staghorn calculus in right half of fused kidney.

Fig. 28. Third degree renal ptosis in a female.

Fig. 29. A, third degree renal ptosis in a male; B, anenrysm of renal artery—diagnosed renal tumor.

Fig. 30. Calculus in left ectopic kidney.

Fig. 31. Painful left ectopic kidney.

Fig. 32. Infected left ectopic kidney.

Fig. 33. Left ectopic kidney and partially calcified retroperitoneal lymph node.

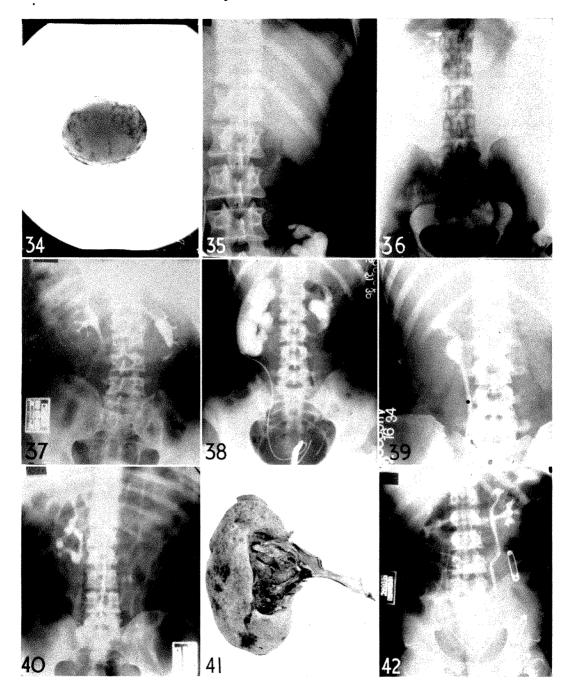


Fig. 34. Partially calcified lymph node (Fig. 33).

Fig. 35. Painful left ectopic kidney.

Fig. 36. Bilateral fused ectopia.

Fig. 37. Incompletely rotated right kidney.

Fig. 38. Incompletely rotated right kidney and abnormal insertion of ureter.

Fig. 39. Absence of some of calyces of right kidney.

Fig. 40. No true renal pelvis—extrarenal ureteral duplication.

Fig. 41. Photograph of removed kidney (Fig. 40).

Fig. 42. Bifid renal pelvis.

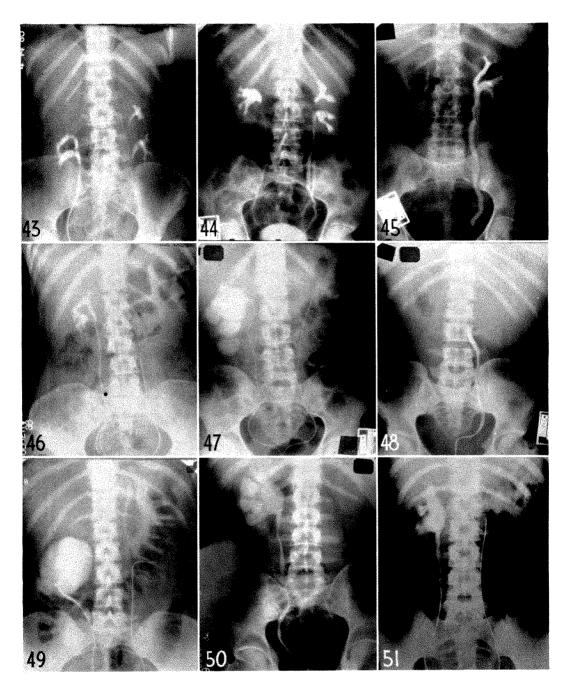


Fig. 43. Bizarre right renal pelvis.
Fig. 44. Duplication of ureter in the distal third.
Fig. 45. Stricture at site of ureteral duplication.
Fig. 46. Duplication of ureter from a juxtavesical position.
Fig. 47. High insertion of ureter to make a surgical kidney.
Fig. 48. Obstruction of ureter from intra-ureteral mucosal valves.
Fig. 49. Hydronephrosis due to congenital ureteral stricture.
Fig. 50. Hydronephrosis due to congenital ureteral stricture.
Fig. 51. Hydronephrosis due to congenital ureteral stricture.

Figure 37 shows an incompletely rotated right kidney with a stone in the renal pelvis; the stone was easily removed through a a pyelotomy. Figure 38 illustrates how incomplete rotation of a right kidney made a poor emptying angle at the ureteropelvic junction and a hydronephrosis; this kidney was removed.

- 6. Anomalies of the calyces, pelvis and ureter are very common.
- (a) Figure 39 shows the right renal pelvis of a female adult which indicates that some of the calyces are absent. A yearly urogram for the past five years has shown the same kind of picture.
- (b) Occasionally there is no true renal pelvis. Figure 40 illustrates a high duplication of the ureter, each branch ending in a major calyx, and for the most part extrarenal. The calculus was in the minor calyx. Figure 41 is a photograph of this kidney and ureter after removal. Note the definite stricture at the point of bifurcation. Figure 42 illustrates a bifid renal pelvis with partial duplication of the ureter. This was an incidental finding in a patient with a ruptured urinary bladder.
- (c) Ureteral duplication is the most common anomaly of the upper urinary tract. Figure 43 reveals a bizarre right double renal pelvis and a left double kidney with duplication of the ureter. The most common site of ureteral duplication is in the upper third. Figure 44 illustrates a right infected double renal pelvis with a duplication of the ureters in the distal third. Occasionally a stricture occurs where the ureters branch; Figure 45 illustrates this point and shows a surgical kidney. Figure 46 shows a right ureteral duplication from a juxtavesical position. When ureteral duplication is complete to make two vesical ureteral orifices for one side, it is important to know that the distal orifice leads to the upper pole of the kidney and the proximal orifice leads to the lower renal pole. This occurs because the upper ureteral bud is pulled below its partner by the faster caudad movement of that portion of the wolffian duct from which it originates.

Anomalous insertion of the ureter at the renal pelvis may produce a pathological kidney. Figure 47 shows a high insertion which caused bad drainage of the renal pelvis; over a long period of time, this produced a surgical kidney in a male adult. Congenital malformations inside the ureteral lumen also cause obstructive uropathy; Figure 48 is the ureterogram of a ureter which contained a set of three muco sal valves at the point of obstruction to make a large, painless but infected surgical hydronephrotic kidney. Figures 49, 50 and 51 illustrate surgical hydronephroses due to congenital ureteral strictures, so termed by the pathologists who examined the removed specimens; all occurred in adults.

(d) Anomalies of size of the ureter are usually associated with infection and the ureterectasis has a definite relation to the infection. Figure 52 shows bilateral dilatation of the lower third of the ureter in a female adult with no apparent obstruction but much infection; the kidneys show moderate pyelectasis. The so-called idiopathic large ureter probably has a defective anatomical and neurological basis. Figure 53 illustrates a huge idiopathic hydrouretero-nephrosis with some dilatation of the opposite ureter in a female adult. Since these dilatations tend to be bilateral, both sides must be studied if surgery is contemplated.

Another anomaly of size of the ureter is illustrated in those patients with ureterocele, which is a cystic dilatation of the lower end of the ureter, with varying amounts of bulbous dilatation of the lower ureter and little or no dilatation of the renal pelvis. Most of these swellings have a very small ureteral orifice. Figure 54 shows the ureterogram of a female adult with a ureterocele, which was discovered when she was examined for a recurrent pyelitis; Figure 55 shows the same finding in a male adult. Ureteroceles may be bilateral and persist over such a long period of time that stasis and infection invite the formation of calculi. Figure 56 illustrates

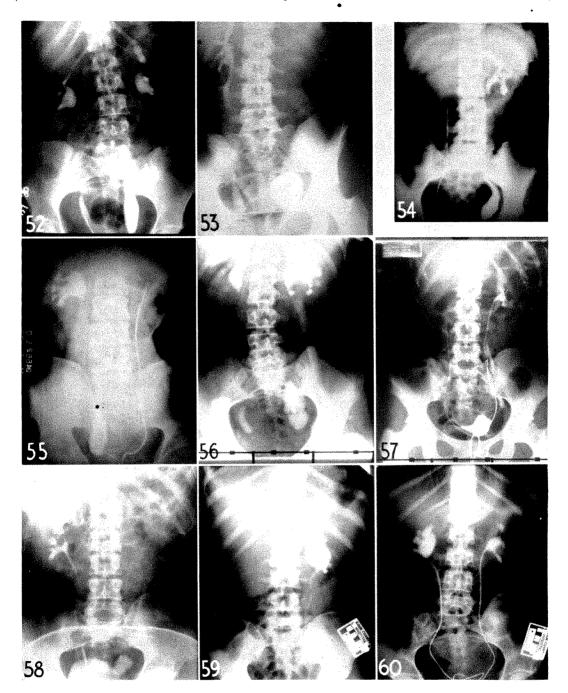


Fig. 52. Idiopathic dilatation of lower ureters.
Fig. 53. Huge idiopathic hydro-ureteronephrosis.
Fig. 54. Left ureterocele in a female.
Fig. 55. Right ureterocele in a male.
Fig. 56. Bilateral ureterocele and multiple urinary calculi.
Fig. 57. Left ectopic ureteral opening into vagina.
Fig. 58. Left ectopic ureteral opening into a seminal vesicle.
Fig. 59. Hydronephrosis and aberrant renal artery.
Fig. 60. Hydronephrosis and aberrant renal artery.

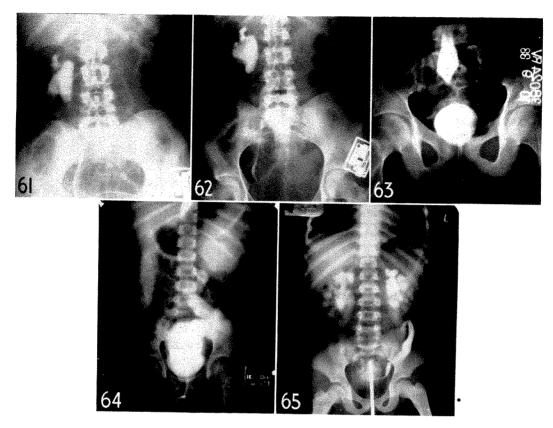


Fig. 61. Hydronephrosis and aberrant renal artery before section of vessel. Fig. 62. Hydronephrosis and aberrant renal artery after section of vessel. Fig. 63. Urachal cvst.

Fig. 64. Hydro-ureteronephrosis and congenital urethral valves in a boy. Fig. 65. Hydro-ureteronephrosis and contracture of the vesical neck in a boy.

bilateral ureterocele formation and calculi in both kidneys and one ureter.

(e) Anomalies of position of the lower end of the ureters may not be discovered until adult life is reached, in spite of the incontinence of urine and much inconvenience. Figure 57 is the urogram of a female adult with a completely duplicated left kidney and ureter, with the lower left ureteral orifice ectopic in the vaginal introitus; the lower end of the ectopic ureter was dilated but the kidney was not infected. The kidney did not lend itself well to a heminephrectomy, so a complete ureterectomy of the ectopic ureter was done with an uneventful recovery. Figure 58 is the urogram of a male adult with complete duplication of the left ureter and kidney but one of the left ureters opens

extravesically into the left seminal vesicle; when indigo carmine is injected intravenously, it appears in spurts from the verumontanum. This patient suffers from a chronic urinary tract infection.

7. One cannot leave the subject of the anomalous kidney and ureter without directing attention to the anomalous blood vessels which supply many kidneys. Whether the aberrant vessels cause pathology is still debatable; however, renal and ureteral symptoms and pathology are found in the presence of aberrant vessels and must, in most instances, be considered related. Figure 59 shows a left hydronephrosis in a male adult which was apparently caused by an aberrant artery; section of vessel gave complete relief from previous symptoms and pyelectasis. Figure

60 illustrates the same finding in a young female adult with periodic acute symptoms; this kidney was removed. Section of an aberrant renal vessel may relieve the symptoms of obstruction without changing the hydronephrotic picture. For example, Figure 61 shows a hydronephrosis and aberrant vessel preoperatively and Figure 62 is the postoperative urogram of the same patient. Care must be used in the section of these vessels; to cut one which supplies too much renal substance invites necrosis of the kidney. It is wiser in some instances to cut and transplant the ureter to a new position of the renal pelvis.

- 8. (a) Regardless of the controversy as to whether the urachus is the remains of the embryological allantois or is sometimes a part of the formed bladder which has been pulled up to the umbilical region, interesting anomalies occur in this region. Figure 63 shows a cyst of the urachal region; there was a constant discharge from the navel but there was no connection with the urinary bladder. The cyst was removed.
- (b) There is some doubt as to whether vesical diverticula are congenital outpouchings which are aggravated by vesical neck obstruction or whether they are blown

out portions of a worn out bladder wall back of a long standing obstruction. The fact that vesical diverticula are found in the newborn has led to the supposition that they could originally be a budding from the wolffian duct, similar to the formation of the ureteral bud. This theory is attractive because almost all diverticula occur in the region of the ureteral orifices.

(c) Anomalies of the vesical outlet are important because of their obstructive character and resulting uropathy. Figure 64 is the urogram of a boy with congenital urethral valves. Note the pyelo-uretero-ectasis of a marked character. Figure 65 illustrates bilateral infected hydro-uretero-nephrosis in a boy, aged eight, with a congenital bar or contracture of the vesical neck; this obstruction was resected with a good clinical recovery.

Time does not permit a complete review of the anomalies of the urinary tract but the above discussion will emphasize the fact that much uropathy occurs in the presence of these anomalies and that urography is indispensable in the diagnosis and treatment of these conditions.\*

\* For discussion see page 657.



## **URETERAL OBSTRUCTION\***

By B. H. NICHOLS, M.D. Cleveland Clinic CLEVELAND, OHIO

TRETERAL obstruction with resultant hydronephrosis should be a subject of the utmost importance to the roentgenologist as such a lesion may produce symptoms easily ascribed to other abdominal complaints or to pathologic change in the spine. Every roentgenologist should think of this possibility in suspected gastroenterological problems, particularly if examination of the spine and gastrointestinal tract is negative. This type of examination is as easily accomplished as an intravenous examination of the gallbladder. By such investigations, many otherwise undiagnosed kidney lesions may be definitely exposed.

Intravenous urography should constitute one of our major methods of examination and should be used as frequently as most other examinations. In a recent review of a great number of cases of ureteral obstruction, we were amazed to find that a high percentage of cases had markedly advanced lesions and that a vast number had been submitted to operations directed to other organs without relief of the symptoms. This applies particularly to patients without abnormal change in the urine or without bladder symptoms.

We hope by this discussion to make more men "kidney conscious," with the result that a correct diagnosis may be made earlier and more often. This is of particular importance when ureteral obstruction is present, either partial, or complete and continuous, or intermittent. Damage to the kidney will result on the affected side, and often infection from retention or the formation of kidney stones, and eventually destruction of a kidney.

In order to appreciate more fully the cause of these changes, it is pertinent to review briefly the anatomy, physiology, and innervation of the ureter. I would like

to impress on the roentgenologist the everincreasing necessity of a better understanding of neurological symptoms which play so great a part in the diagnosis of almost all diseases. This applies particularly to pain and its distribution. The ureter is a flattened tube which extends from the outlet of the kidney pelvis to the angle of the vesical trigone where it empties into the bladder. It may enter the bladder at almost a right angle to the wall or it may enter in a rather marked oblique course. The ureter is composed of three coats—a fibrous outer coat, a muscular middle coat, and an inner epithelial coat or mucosal lining—underneath which lies a layer of submucosal tissue composed of elastic fibers and connective tissue. The middle or muscular coat is composed of unstriped

The vascular supply of the ureter is abundant, being derived from several sources, and it is freely anastomosing. The renal artery supplies the upper third of the ureter; branches from the aorta and common iliac, the inferior mesenteric or spermatic supply the middle third, while the lower third is supplied from the vesical arteries and the vas.

The nerve supply of the ureter is also very important in ureteral obstruction and particularly in the study of referred pain. The nerve supply is an intricate meshwork of small fibers. The outer fibrous sheath of the ureter carries the nerve supply, the innervation coming mainly from the renal, spermatic, ovarian, and hypogastric plexuses. The vesical plexus also supplies a portion of the lower end of the ureter. The afferent fibers come from the tenth and eleventh thoracic vertebrae, and the first lumbar vertebra. The efferent fibers are also in the vagus supply to the ureter. A few ganglia are found in the lower third of

<sup>\*</sup> Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19-22, 1939.

the ureteral segment. The definite anatomical structure of the innervation of the ureter, however, has not been accurately demonstrated. It is interesting experimentally, however, that all the nerves supplying the ureter may be cut and yet its contractions appear to continue normally. Even a cut section, completely taken from the ureter, is seen to contract rhythmically after removal, and little influence can be induced in the ureter by stimulation from the hypogastric nerves or by the administration of adrenalin. There is no sphincter at the lower end of the ureter; apparently it is closed by the contraction of the bladder wall and, it is believed, by a reflex contraction of the lower portion of the ureter.

The results of partial or complete obstruction to the ureter must be understood if correct diagnoses and treatment are to be instituted. It has been shown that, if the ureter is completely obstructed permanently, atrophy and nonfunction of the kidney take place. Intermittent or partial obstruction results in a marked dilatation of the kidney, causing hydronephrosis and accompanying pain and urinary stasis which results in infections and often in the formation of renal calculi.

From a clinical standpoint, pain is usually the first symptom of any degree of obstruction that overdistends the pelvis of the kidney. Because such pain may be referred to the gastrointestinal tract and simulate spastic colon, or to the region of the gallbladder simulating gallbladder colic, and because it may simulate lesions of the spine, angina pectoris, and many other symptoms, the pain of hydronephrosis may continue for a long time before its true etiology is determined. It may be stated quite truthfully that hydronephrosis may present no characteristic symptoms and may be recognized only by inference. Therefore, one should always bear in mind the possibility that such a condition may be present. Since early hydronephrosis may cause no abnormal change in the urine, attention is often not

directed to the possibility of ureteral obstruction.

For a number of years it has been our policy to make a careful examination of the abdomen in order to determine the size and shape of both kidneys, as well as the presence or absence of visible calculi before any examination is made with opaque media for a study of the gallbladder or gastrointestinal tract. It has been possible by this procedure to determine in a large number of cases the presence of a stone. either in the kidneys or ureter, which had heretofore been unrecognized, to discover the presence of a tumor of the kidney as shown by the abnormal change in the contour of this organ, and also to determine the presence of a large kidney on one side suggesting the presence of hydronephrosis. We consider this procedure to be very important and we advise that all patients who are suffering from abdominal pain have such an examination made as the first roentgenological diagnostic procedure.

The causes of ureteral obstruction are many. Among the more frequent causes may be considered:

- A. Lesions of the kidney
  - 1. Renal calculi
  - 2. Tumor
  - 3. Infections
  - 4. Blood clots
  - 5. Anomalous renal vessels
  - 6. Anomaly of position
  - 7. Duplex kidney
  - 8. Fused kidney
- B. Lesions of the ureter
  - I. Ureteral calculi Opaque

Nonopaque

- 2. Stricture
- 3. Tumors

Primary

Secondary

4. Trauma

Ligation

Cutting

5. Infection

6. Adhesion

Congenital Acquired

- 7. Kinks
- 8. Congenital valves
- 9. Diverticulum
- 10. Duplication
- 11. Transplanted ureters
- 12. Ureterocele
- 13. Atrophic ureter
- 14. Megalo-ureter
- 15. Ectopic ureter
- 16. Extrinsic pressure
- 17. Pregnancy
- C. Lesions of the bladder
  - I. Tumors
  - 2. Diverticulum
  - 3. Infarction
  - 4. Trauma

The lesions of the kidney offer a special group for diagnosis as many of these ureteral obstructions are secondary to a primary lesion in the kidney. These examinations



Fig. 1. Female, aged fifty-two. Bilateral pyelogram shows a normal right kidney with a large tumor mass in the lower pole of the left kidney producing some intermittent obstruction and a moderate hydronephrosis. Postoperative diagnosis was solitary cyst of the kidney.

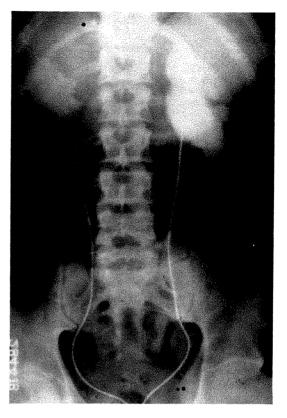


Fig. 2. Male, aged thirty-one. Retrograde pyelogram shows a large hydronephrosis of the left kidney due to an aberrant vessel obstructing the upper end of the ureter. Operation: nephrectomy. The kidney was almost totally destroyed.

will be better made by a pyelogram of the kidney by the retrograde method. Some tumors (Fig. 1) and anomalies such as aberrant vessels (Fig. 2), fused kidneys and malposition will usually be readily diagnosed from a urogram made by the excretory method providing there is a reasonable function in the kidney on the affected side. Hematuria may offer a difficult problem. Repeated examinations or examination during intervals of nonbleeding will often be necessary.

It is a foregone conclusion that most ureteral obstructions must be accompanied by pain during the attacks of distention of the kidney pelvis. If there is complete continuous obstruction, the kidney will cease to function and there may be no pain present due directly to the ureteral obstruction. If, however, there is an accompanying



Fig. 3. Female, aged thirty-nine. Retrograde pyelogram shows a fused ectopic kidney with bilateral ureteral obstruction.

kidney lesion, pain may be present from this source. It is also possible for a tumor of the kidney to be present without pain or hematuria, the latter being absent in about 53 per cent of kidney tumors in our series.

The poor function of polycystic kidneys will often make it impossible to determine the presence or absence of this disease, and retrograde pyelography will be necessary. A fair estimate of function will be determined, however, by the excretory urogram. The fused kidney (Fig. 3) offers obstruction to the ureters by pressure on the upper third and may be accompanied by a chain of symptoms, the so-called horseshoe kidney syndrome described by Gutierrez.<sup>1</sup>

Horseshoe syndrome

a. Abdominal pain in the epigastrium or the region of the umbilicus

- b. Chronic constipation with or without gastrointestinal disorder
- c. Urinary disturbance

Renal calculi (Fig. 4) will often be best apprehended by excretory urograms and the degree of ureteral obstruction determined from the presence of distention or retention at the one hour period. At the same time, the position of the stone will be seen and its location established, while often the retrograde pyelogram will entirely obscure the stone shadow.

This briefly surveys the best plan of examination in the presence of the lesions confined to the kidney. In the majority of all these lesions other methods of examination are helpful and should be done. Certainly, in any questionable case, excretory urography should be followed by a



Fig. 4. Male, aged forty-six. Low back pain for six months. Excretory urogram at thirty minute period shows exact location of a stone in the right kidney pelvis with a little hydronephrosis in the kidney.

retrograde pyelogram. For examination of lesions in the ureter, both catheterization of the ureter and pyelo-ureterograms may be necessary as excretory urography will not often visualize the ureter well. The presence of retention and obstruction and interference of the dynamics of the ureter will be clearly determined, however, and further study of the ureter can be made.

In the examination of a patient with ureteral calculi (Fig. 5), if there is not a complete obstruction by the stone and a functioning kidney is present, excretory urography often offers all the diagnostic information necessary before manipulation or operation is undertaken. The neurological findings of pain and distribution are of aid in locating a nonopaque stone which may also be determined by a nonopaque shadow either in the kidney pelvis or in the ureter, care being taken to exclude an air



Fig. 5. Male, aged thirty-seven. Right ureteral stone. Urogram shows hydronephrosis, intermittent ureteral obstruction. The urogram, one hour period.

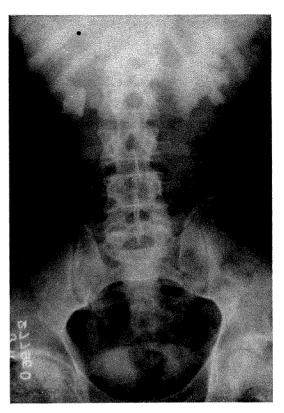
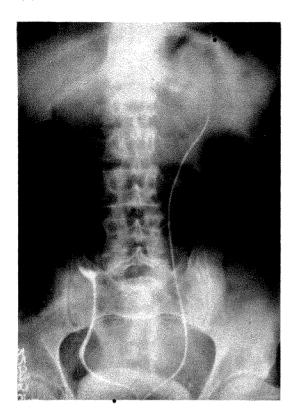


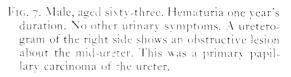
Fig. 6. Male, aged thirty-four. Stricture of left ureter at ureteropelvic junction. Ureterogram shows partial obstruction with a large hydronephrosis. Plastic operation done. Excretory urogram at thirty minute period.

bubble which may be introduced with the pyelographic medium.

Ureteral stricture (Fig. 6). This lesion probably occurs more often in the middle or lower portion of the ureter and may produce partial or complete obstruction. Urologists disagree somewhat on the frequency of occurrence of this lesion. We believe, however, that the presence of spasm of the ureter or spastic contraction may often be mistaken for an organic stricture. We have proved that such was the case where catheter obstruction, suggesting a stricture, was ruled out by a later urogram with four films, showing the suspected area in the ureter to be normal and with no evidence of dilatation of the kidney pelvis, ruling out any apparent ureteral obstruction.

Ureteral tumors, primary or transplant





lesions (Fig. 7) produce obstruction of the ureter with an accompanying hydronephrosis and hematuria and in the trans-

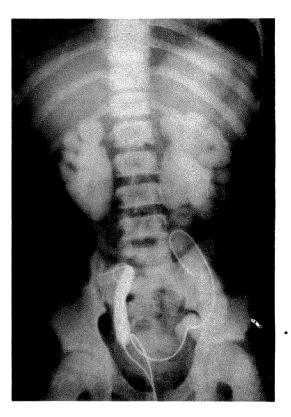
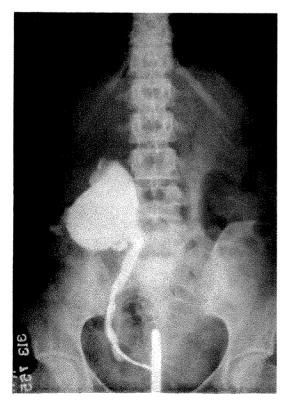


Fig. 9. Male, aged fifteen. Retrograde pyelogram showing bilateral hydronephrosis, bilateral ureterectasis, with bilateral congenital valve at the lower end of the ureters. Patient has renal rickets.



plant lesion a primary tumor will be found in the accompanying kidney.

Trauma, either injury or surgical accident or radiation stenosis, may safely be studied by excretory urography if extravasation is present; although the kidney may rupture, no harm can be done.

Fig. 8. Female, aged thirty-four. Diagnosis, ureteral obstruction at ureteropelvic junction. Pyelonephrosis right kidney. Urinary symptoms one year. Operation: nephrectomy.

Fig. 11. Male, aged fifty-four. Cystogram shows diverticula of bladder with one diverticulum near the lower ureteral orifice on the left, producing partial obstruction to the ureters.

Ligated or crushed ureters show no function.

Infections (Fig. 8). Most infections will be accompanied by pus in the urine and frequently by blood. Such cases are best



F16. 10. Male, aged seventy-six. Excretory urogram at thirty minute period shows the right kidney with a double ureter and kidney pelvis and hydronephrosis.

examined by a catheterization of ureters and retrograde pyelogram.

Adhesions to the upper ureter may simulate very closely an aberrant vessel obstruction at the ureteropelvic junction and it will be found impossible in many cases to

Fig. 12. Male, aged fifty-nine. Catheterization of right ureter with a ureteropyelogram, showing a large ureterocele at the lower end of the right ureter, producing partial obstruction of the ureter.





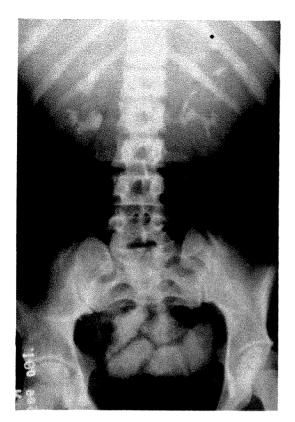


Fig. 13. Transplanted ureters (transplanted at nine years of age). Female, aged twenty-nine. Both kidneys apparently normal size with good function. Large quantity of urine and dye in colon showing good retention.

differentiate between these lesions by roentgen examination. Kinks and congenital valves will be well visualized by the excretory urogram; ureteral valves (Fig. 9) are usually bilateral and if catheterization of the ureter is done the catheter will be introduced into the ureter from below unobstructed.

Duplication of the ureter (Fig. 10), if not completely to the bladder, will often produce a partial obstruction at the joint of bifurcation confined usually to one leg of the bifurcation. It will usually be necessary to do a ureteropyelogram to visualize well such a lesion.

The excretory urogram is often the procedure that shows a double kidney pelvis and will be the first suspicious finding.

Diverticulum (Fig. 11) and ureterocele (Fig. 12) are both rare lesions and can

usually only be found by a retrograde pyelo-ureterogram. However, they should be kept in mind and if any unusual finding arises on an excretory urogram, instrumental urography should immediately be recommended.

Transplanted ureter with obstruction can only be studied by excretory urograms (Fig. 13); also this is the best method for the examination of the dilatation of the ureter in pregnancy, The atrophic obstruction of the ureter in polycystic kidneys is difficult to detect at all by excretory urograms as usually these kidneys have a poor function. The ectopic ureter will require a retrograde pyelogram or ureterogram.

Megalo-ureter will usually be visualized well by the excretory urogram. Extrinsic pressure on the ureter will also usually be determined well by the excretory urogram. Many lesions of the bladder are best in-

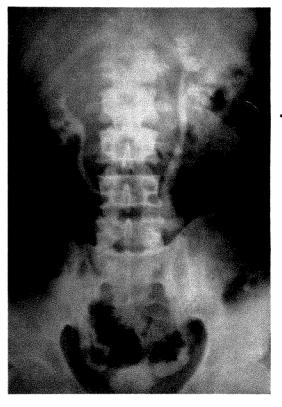


Fig. 14. Male, aged thirty-four. Urinary symptoms for three years. Miliary tuberculosis of the lungs. Tuberculosis of the bladder with urinary obstruction. Excretory urogram at thirty minute period.

vestigated by cystoscopic examination, except for possible diverticula. In the presence of a diverticulum with the ureter entering such a lesion, a cystogram will often be of greatest aid. Tuberculosis of the bladder may be studied by a urogram (Fig. 14).

This brief consideration of ureteral obstruction will call attention to the great variety of possibilities and call our attention to the necessity of thorough examination, if the roentgenologist is to become a proficient diagnostician.

The urologist will be the judge as to diagnosis and management. The clinical history and the urological findings combined with roentgenological findings are all necessary in the final diagnosis.

## DISCUSSION OF PAPERS BY DRS. GILLIES, BAKER, AND NICHOLS

DR. HERMAN L. KRETSCHMER, Chicago. The essayists have covered the various assignments in a very thorough and comprehensive manner. I should like to discuss these papers from the point of view of some of the diagnostic problems that I have met in this particular field. I will illustrate my remarks with lantern slides.

slides.
(Slide) We are generally accustomed to kidney, certain more or less characteristic changes are found in the pyelogram and this impression as a broad, general proposition is true. On the other hand, one may occasionally see a patient who has a tumor of the kidney and the pyelogram is normal. In this case an infant had a tumor of the kidney that in its growth did not invade nor compress the renal pelvis and the pyelogram as you see was normal. I think one must bear this possibility in mind so as not to come to wrong conclusions. This was a Wilms' tumor, and, as I said before, it had not compressed nor invaded the kidney pelvis; hence the pyelogram was normal, so unless we think of this remote possibility, we are likely to be led astray.

(Slide) This slide shows a double kidney pelvis and a double ureter, of which you have seen many examples this morning. The reason I show this slide is to call your attention not to this anomaly *per se*, but to the frequency with

which it is incorrectly diagnosed. Patients who have this aromaly are told that they have an extra kidney and cases of this type have been diagnosed as supernumerary kidneys. Supernumerary kidneys mean the presence of three separate and distinct kidneys. These patients do not have three kidneys. They have two kidneys. They have a double kidney on one side and a normal kidney on the other and at other times the lesion is bilateral, several examples of which we have just seen. It is interesting to note how frequently cases are reported as supernumerary kidneys when the author's illustrations clearly show that he is reporting cases of double kidney.

(Slide) This is a case of true supernumerary kidney. On this side the pyelogram is normal. On the opposite side you will note that there are two separate and distinct pelves widely separated. This patient actually had three separate and distinct kidneys with a free interval between them. The kidneys were not connected as is the case in double kidney. This diagnosis was verified by operation. As you all know, these cases are very rare; nevertheless we should be accurate in the use of descriptive terms, when reporting cases of this kind.

(Slide) There seems to be a little difficulty at times in the diagnosis of polycystic kidney. Polycystic kidney has frequently been confused with malignant tumor. Occasionally it is quite difficult especially in the early cases to make the differential diagnosis. One must also bear in mind the fact that the patient with a polycystic kidney may occasionally have a malignant tumor in that polycystic kidney. There should be no difficulty in recognizing this as the pyelogram of polycystic kidney.

(Slide) Most urologists believe that they are always bilateral. Here is a pyelogram from which a diagnosis of polycystic kidney was made elsewhere and the patient treated for several years as a case of bilateral polycystic disease of the kidney. This patient has a peculiar pyelogram but careful study of this pyelogram shows that there is a trickling of the medium toward the upper pole and one should have no difficulty in diagnosing this a malignant tumor. A diagnosis of hypernephroma was made and verified by operation. The patient subsequently died of brain metastasis. The point is, this was a pyelogram of a tumor incorrectly diagnosed as a polycystic kidney, and the patient was treated medically for three or

four years before the final and correct diagnosis was made.

(Slide) This shows an intravenous urogram and it is an exceedingly interesting one. One is at once impressed by the great length of the pyelograms as well as by the somewhat bizarre appearance. A large easily palpable mass was present in both right and left upper quadrants. The patient, a child, had a splenomedullary leukemia with leukemia infiltration of both kidneys, which accounted for these peculiar pyelograms. I show them because of their close resemblance to the pyelograms of a polycystic kidney with which condition they might be confused.

(Slide) Occasionally the problem of differential diagnosis may arise between tumors of the kidney and retroperitoneal tumors. In this group of cases one must resort to the use of the cystoscope, ureteral catheters and pyelograms. In this instance the patient had a peculiar shadow, as you can see it was irregularly dense. There was displacement of the ureter. At operation a retroperitoneal lipo-fibrosarcoma was found.

(Slide) This is the pyelogram of another patient with a retroperitoneal tumor and it shows in a very clearcut manner the displacement of the ureter as a result of the growth of the tumor. Displacement of the ureter is relatively frequent in cases of retroperitoneal tumor.

(Slide) Attention was called this morning to the fact that the presence of blood clot in the renal pelvis may be confused with tumor of the pelvis or tumor of the kidney proper. In this patient the filling defect was due to the presence of a very large blood clot in the kidney pelvis.

(Slide) Sometimes a differential diagnosis between a solitary cyst and malignant tumor of the kidney may be exceedingly difficult. In some of the cases of solitary cyst the intravenous urolograms show progressive increase in the density of the shadow produced by the cyst after the cyst becomes filled with the contracting fluid. Unfortunately, this is not always present. A filling defect produced by a solitary cyst many times closely resembles the filling defect produced by a tumor.

Dr. T. P. Grauer, Chicago. In regard to malignant tumors, the films that were shown and demonstrated were very beautiful and, in most instances, very obvious. The thing that seems important to me is that in many in-

stances urological pictures do not clearly show a malignant tumor of the kidney when such a tumor is present. In other instances an obvious diagnosis from the picture or pyelogram may cause one to miss a tumor which is present.

Dr. Jenkinson will bear me out on these two cases, which I will mention briefly. About four years ago we saw a patient with a mild, spontaneous hematuria with no other symptoms. The patient was cystoscoped and pyelographed to find the source of the bleeding and on the pyelograms, which were very good, no lesion could be found except a hydronephrosis on the right side. The examination was repeated. Still no other lesion could be found and the patient was discharged from the hospital. About a year later he fell on the ice and was brought back into the hospital in more or less shock, with another hematuria following this fall. At this time he had ruptured a large hypernephroma of this kidney. We went back and looked at the roentgenograms which had been taken a year before. One calyx of this large hydronephrosis did look just a little bit frayed and a little bit fuzzy.

The other case that I want to mention is a case of a woman who came to us because she had some pus in her urine, occasionally a little hematuria, and a high temperature. Pyelograms and cystoscopic examination at that time revealed four or five large stones in the lower end of the megalo-ureter. This was also markedly affect. ing the ureter. A ureteronephrectomy was performed and a papillary tumor was demonstrated which could not be shown on the pyelograms. The patient subsequently died of metastases from this tumor. So we do not always want to think about the obvious. Sometimes one must look a lot closer and not be content with the obvious diagnosis from the roentgenograms.

When one reads the title of the third paper, "Ureteral Obstruction," most of us think immediately of ureteral strictures, and ureteral strictures are a matter of geography more or less. In the East the urologists see a great many more ureteral obstructions than we do and I think possibly that is due to the influence of urologists in those regions. One thing that Dr. Nichols brought cut, and with which I agree heartily, is that a great many ureteral and renal lesions have predominant abdominal or gastrointestinal symptoms, and I think most of us should think more often of kidney and ureter pathology in vague abdominal symptoms.

## PYELOVENOUS BACKFLOW

By WALTER L. KILBY, M.D.

From the Department of Roentgenology, University of Maryland Hospital Baltimore, Maryland

THE term "pyelovenous backflow" is generally used today to describe a fascinating phenomenon demonstrated occasionally on the retrograde pyelogram as an extravasation of opaque material into the venous system of the kidney. The phenomenon is not only fascinating but is important in the study of the circulation of the kidney, in the realization of the damage that may be done to the kidney during retrograde pyelography, and in the interpretation of pyelograms. Investigation of the phenomenon has thrown considerable light upon the venous, arterial, and ---lymphatic systems of the kidney. The extravasation of opaque medium and possibly infected urine into the blood stream may graphically explain reactions following retrograde pyelography which at times lead to a rise in temperature, sepsis, and possibly death. The characteristic findings of pyelovenous backflow on the roentgenogram have many times been erroneously interpreted by both urologists and roentgenologists as tuberculosis, tumors, and other forms of kidney extravasation and infection.

Voelcker and Lichtenberg<sup>14</sup> in 1906 were the first to demonstrate the practicability of outlining the urinary tract with opaque substances. The early use of silver salts as opaque substances and the subsequent demonstration of the ease with which these substances could be forced into the blood stream made retrograde pyelography somewhat of a hazardous procedure. The use of sodium iodide in subsequent years eliminated somewhat the reactions following pyelography but with the use of the halogenated organic substances of today such as hippuran, skiodan, and neoiopax, only rarely are difficulties encountered.2 Renal pelves may be perforated by catheters, this being more easily done in children than in adults. The walls of the pelvis and ureter may be ruptured by pressure, particularly if weakened by infection, stones, or ulceration.<sup>13</sup>

Extravasation of opaque material into the kidney may be divided into four types: (1) pyelolymphatic backflow, (2) pyeloparenchymatous backflow, (3) pyelotubular backflow, and (4) pyelovenous backflow. Roentgenologists have a tendency to classify extravasations into only two types, pyelovenous backflow and the interstitial type. That pyelotubular and pyelolymphatic backflows also occur there is very little doubt and an effort should always be made to differentiate these various types.

The rarity of the demonstration of pyelolymphatic backflow is evidenced by the fact that up to 1937 only 15 cases had been reported, at which time Campbell and Seidler<sup>6</sup> added 2 additional cases. Roentgenologically pyelolymphatic backflow is recognized as irregular, tortuous, linear shadows 2 or 3 mm. in diameter extending from the kidney medially toward the spine. Occasionally these injected vessels appear to begin in the corticomedullary zone and extend medially past the pelvis toward the spine and then curve slightly downward. No marked pressure is required to produce pyelolymphatic backflow.

Chyluria is usually attributed to a blockage of the thoracic duct by the tropical parasite, *Filaria sanguinis hominis*, in the absence of an adequate collateral lymphatic circulation. Non-parasitic chyluria rarely occurs also. The exact mechanism whereby chyle reaches the urinary tract has never been satisfactorily explained; however, it is supposed that where there is an obstruction to the thoracic duct chyle passes retrogradely down the lym-

phatics that drain the kidney. Dilatation and stasis of the perirenal lymphatics occur which subsequently rupture into the urinary tract producing chyluria.1 Some investigators have suggested the presence of lymph stomata in the pelvis but these have never been histologically or anatomically demonstrated. Hampton<sup>8</sup> in 1920 first reported a case of pyelolymphatic backflow with non-parasitic chyluria which was not clearly demonstrated on the pyelogram. Wood<sup>15</sup> in 1928 was the first to demonstrate clearly pyelolymphatic backflow on the pyelogram in a case of non-parasitic chyluria. In all cases of chyluria an attempt should be made to demonstrate pyelolymphatic backflow by retrograde pyelography and whenever pyelolymphatic backflow is demonstrated, chyluria should be suspected. Since chyluria may be intermittent, several specimens of urine should be examined.

Pyelotubular backflow has been a much discussed phenomenon. The findings of some workers seem to indicate with little doubt that this type of backflow actually occurs at times although their work has not always been confirmed. O'Conor<sup>13</sup> found that silver nitrate and mercurochrome could be forced up the collecting tubules to the glomeruli. Mason<sup>10</sup> in 1914 showed that substances could be made to ascend into the straight and convoluted tubules and into the glomeruli, this work being confirmed by Burns and Swartz<sup>5</sup> in 1918. Hinman and Lee-Brown<sup>9</sup> in 1924, using 2 per cent Berlin blue, were unable to demonstrate tubular reflux to any degree in fresh human kidneys even after using considerable pressure, while about two vears later Bird and Moise<sup>3</sup> showed that India ink could be passed readily through the renal tubules to Bowman's capsule under pressures varying from 10 mm. of mercury to 100 mm. of mercury. They found little evidence of venous extravasation of the India ink, a finding somewhat opposed to the work of Hinman and Lee-Brown.

Since 1926 it has been found that pyelo-

tubular backflow does occur at pressures usually used in clinical pyelography. The characteristic appearance of pyelotubular backflow is the short brush-like radiation extending outward into the medulla from the calyces for a distance of 5 or 6 mm. Occasionally pyelovenous and pyelotubular backflow occur simultaneously.

Pyeloparenchymatous backflow occurs following retrograde pyelography with pressures ordinarily used in filling the upper urinary tract. This interstitial type of extravasation is usually seen on the pyelogram as an irregular distribution of the opaque material in the medullary zone, about the major and minor calvees, about the pelvis, under the capsule, in the perirenal tissues, or along the upper portion of the ureter. This type of extravasation is more apt to occur with the use of the syringe method than with the gravity method. It may or may not be associated with pain in the kidney region and is frequently followed by bleeding from the involved side. Chills, fever, and even perinephric abscesses may follow this type of injury to the kidney.

In 1938 Narath<sup>11</sup> reported the first and only case of extrarenal extravasation from the renal pelvis during intravenous pyelography. This case showed no evidence of obstruction and the pelvis and calyces were never completely filled. There was no history of trauma to the kidneys. The occurrence of extravasation during intravenous pyelography and with such low intraureteral pressures during retrograde pyelography indicates the ease with which this type of accident may occur.

The subject of venous extravasation was brought to the attention of the medical profession by Hinman and Lee-Brown at the annual meeting of the Americal Medical Association in San Francisco in 1923 at which time they were awarded the Gold Medal for an exhibit showing this phenomenon. They chose to call this phenomenon "pyelovenous backflow." These workers found, by injecting postmortem kidney specimens of humans, sheep, dogs,

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and rabbits, using moderate intrapelvic pressures, that the pelvic contents passed back into the renal veins. The pressures used were always below maximal secretory pressures and gross and microscopic studies showed no evidence of local rupture. By using anesthetized sheep and dogs with the ureters exposed, they were able to demonstrate roentgenographically and by sections pyelovenous backflow following injection with sodium iodide solution and 2 per cent Berlin blue solution at pressures as low as 20 mm. of mercury.

In order to appreciate the problem of pyelovenous backflow one must have some knowledge of the vascular system of the kidney. The renal artery ordinarily possesses three branches which pass up into the hilum and ramify through the interstices forming interlobar and arcuate arteries. From the arcuate arteries fine radial branches pass at right angles to the renal surface to supply the cortex. The arterial supply is an end one, there being no anastomosis.

The fine radially fashioned interlobular veins begin in the cortex and pass inward forming anastomosing arcades at the corticomedullary zone. From these arcades spring interlobar veins which pass downward toward the hilum next to the wall of the calyces and frequently in contact with the mucosa of the calyces. In the region of the fornices of the calyces the interlobar veins arch around the pyramids and it is at this point that most investigators feel that pyelovenous backflow first begins. The interlobar veins collect into usually three branches of the renal vein.

The mechanism of pyelovenous backflow has not, even up to today, been satisfactorily explained. Levin¹ in 1903 thought that possibly there existed natural communications between the renal pelvis and the venous system. Hinman and Lee-Brown in 1924 felt that distention of the calyces produced a spreading of the fornices between the calyces and the papillae resulting in minute ruptures into the adjacent rich venous plexus. Bird and Moise

in 1926 suggested that the reflux first occurred up the collecting tubules and then ruptured into the adjacent interlobular veins. This explanation seemed to be somewhat disproved in 1927 by Brown<sup>4</sup> who showed that the hypodermic injection of India ink into the cortex of fresh kidneys resulted in the filling of the venous capillary system with very little being found in the tubules. This fact seemed to show that the venules were much more fragile and subject to rupture than the tubules. Fuchs<sup>7</sup> in 1930 believed the extravasation occurred in a perivenous fashion before there was a final rupture into the veins.

It is quite surprising to see pyelovenous backflow, as well as the other types of renal and perirenal extravasation, following the use of such low pressures. Scott<sup>12</sup> in 1933 in connection with the study of effects on the pyelogram of various pressures found that great pressure of the injected medium does not enlarge the pyelographic shadow beyond that of a normally filled one. This would seem to eliminate the impression that apparent dilatation of the upper urinary tract is due at times to overdistention and not to hydronephrosis. Scott also found that 25 per cent of 162 injected postmortem specimens, using 30 mm. of mercury pressure, showed pyelovenous backflow and that shape and disease of the pelvis played no part in the occurrence of this phenomenon.

In the pyelogram pyelovenous backflow is seen as cone-shaped funnels beginning just beyond the minor calyces. In the corticomedullary zone, arcades of anastomosing veins may be seen from which extend into the cortex radiations of opaque material. Pyelotubular backflow is always in the form of short brush-like tufts extending out from the tips of the calyces. Arcades and cortical radiations are never seen in pyelotubular backflow. It also must be remembered that both pyelotubular and pyelovenous backflow may occur simultaneously.

The following case is presented for it represents a phase of pyelovenous backflow



Fig. 1. A right retrograde pyelogram with an opaque catheter in the right ureter shows irregularity of the calyces and extravasation of the opaque medium indicative of pyelovenous backflow. The areas of increased density in the right side of the abdomen are extra-ureteral.

occurring in the living human that has not been described before.

White, unmarried female, aged fifty-eight. Admitted to the University of Maryland Hospital January 5, 1939 complaining of soreness in the right lumbar region and pain in the right upper quadrant of the abdomen. The patient complained of nocturia of three times for many years. No hematuria, pyuria, burning, tenesmus, or frequency present. The patient had been seen in a private office a few days before admission and had had a plain film of the kidneys, ureters, and bladder. On the film two areas of increased density were seen on the right which suggested ureteral calculi.

The physical examination showed moderate obesity, a blood pressure of 192/112, and tenderness over the 12th right rib.

Blood and urinary studies were normal. Phenolsulphonphthalein excretion was 90 per cent in two hours. Non-protein nitrogen in the blood was 27 mg. per 100 cc. of blood. Wassermann reaction negative.

Cystoscopy showed the urethra normal; bladder was normal. Moderate trigonitis present. Right ureter catheterized easily with a No. 5 catheter. A No. 5 catheter could not be passed up the left ureter. A plain film with the catheter in the right ureter showed the areas of increased density not in relation to the catheter. With a syringe 18 cc. of skiodan was injected in the right pelvis. The pyelogram showed the areas of increased density to be not in the ureter. Considerable pyelovenous backflow had occurred. The pelvis was refilled about twenty minutes later and a film was made. Less pyelovenous backflow occurred on the right but a pyelogram of the left kidney was also seen,

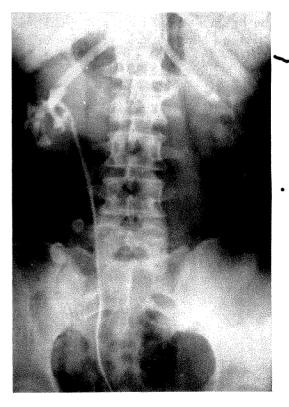


Fig. 2. The right kidney pelvis was reinjected. The film was made about twenty minutes after the first injection as indicated in Figure 1. The extravasated dye has disappeared. The calyces appear sharper in outline. At this time a pyelogram is noted on the opposite side, evidently due to excretion of the dye that had been extravasated into the vencus system on the right side at the time of the first pyelogram.

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evidently due to excretion of the extravasated dye on the left. No bleeding occurred after the pyelovenous backflow and there was no post-cystoscopic reaction.

The only analogous phenomenon found in the literature occurred in the experimental work of Hinman and Lee-Brown in 1924. These workers exposed the ureters of an anesthetized sheep, filled one pelvis with a solution of phenolsulphonphthalein at 40 mm. of mercury pressure and shortly phenolsulphonphthalein appeared in the urine from the opposite kidney. Subsequent examination of the kidneys showed no rupture or extravasations.

The appearance of dye in the opposite kidney shows without doubt that pyelovenous backflow actually occurred. This graphic demonstration might be more often observed if additional films were routinely made ten or fifteen minutes after discovery of pyelovenous backflow.

#### SUMMARY

- 1. The four types of kidney extravasation are reviewed and their differential characteristics are pointed out.
- 2. The case of pyelovenous backflow presented adds new evidence that venous extravasation occurs.

The privilege of reporting this case, granted by Dr. J. Mason Hundley, Professor of Gynecology, University of Maryland, Baltimore, Maryland, is acknowledged.

#### REFERENCES

 ABESHOUSE, B. S. Pyelographic injection of the perirenal lymphatics. Am. J. Surg., 1934, 25, 427-450.

- BARETZ, L. H. Rupture of kidney following pyelography. J. Am. M. Ass., 1936, 106, 980-983.
- 3. BIRD, C. E., and Moise, T. S. Pyelovenous backflow. J. Am. M. Ass., 1926, 86, 661-663.
- 4. Brown, R. K. L. Phenomenon of pyelovenous backflow. J. Urol., 1927, 17, 105-112.
- 5. Burns, J. E., and Swartz, E. O. Absorption from the renal pelvis in hydronephrosis due to permanent and complete occlusion of ureter. J. Urol., 1918, 2, 445-454.
- CAMPBELL, M. F., and SEIDLER, V. B. Urographic pyelolymphatic backflow. Am. J. ROENTGENOL. & RAD. THERAPY, 1937, 38, 602-606.
- 7. Fuchs, F. Pyelovenous backflow in human kidney. J. Urol., 1930, 23, 181-216.
- 8. Hampton, H. H. A case of non-parasitic haematochyluria. *Bull. Johns Hopkins Hosp.*, 1920, 31, 20.
- HINMAN, F., and LEE-BROWN, R. K. Pyelovenous back flow, its relation to pelvic reabsorption to hydronephrosis and to accidents of pyelography. J. Am. M. Ass., 1924, 82, 607-613.
- Mason, J. M. Dangers attending injections of the kidney pelvis for pyelography. J. Am. M. Ass., 1914, 62, 839-844.
- II. NARATH, P. A. Extrarenal extravasation observed in course of intravenous urography. J. Urol., 1938, 39, 65-74.
- 12. Scott, D. E. Effects of pressure of pyelographic mediums. *J. Urol.*, 1933, *30*, 39–47.
- 13. Stevens, W. E. Roentgenologic examination of kidney with special reference to backflow and injuries associated with retrograde pyelography. J. Urol., 1938, 39, 598-610.
- 14. VOELCKER, F., and LICHTENBERG, A. Pyelographie (Roentgenographie des Nierenbeckens nach Kollargolfüllung). München. med. Wchnschr., 1906, 53, 105-107.
- WOOD, A. H. Unilaterial renal chyluria. J. Urol., 1929, 21, 109-117.



### LATERAL PYELOGRAPHY\*

By E. L. SHIFLETT, M.D., and D. Y. KEITH, M.D. LOUISVILLE, KENTUCKY

THE lateral pyelogram is an aid to the study of pathologic behavior. It is not recommended as a routine examination but it is frequently indicated and sometimes necessary. We will not attempt to establish diagnostic dogma but will discuss briefly our experiences with lateral pyelography during the past five years.

#### TECHNIQUE

The lateral pyelogram is made on the regular cystoscopic table. The patient must



Fig. 1. Position of kidney and ureter normal for this individual. Ureter slightly forward at level of lumbosacral joint because of catheter tension.

be in an exact lateral position with the questionable side next to the film. The side uppermost is subject to considerable distortion. The ureter and/or kidney is refilled, depending on whether a ureteropyelogram or pyelogram is desired, and roentgenographed with the shortest possible exposure. The roentgenogram should

visualize the usual quantity of pyelographic medium or leaded catheter in the ureter and kidney. Occasionally, in large individuals, an increase in concentration of the pyelographic medium permits better visualization. The catheter may be left in the opposite ureter when for some reason it is advisable to do so. The best results are obtained by retrograde technique, but in those pathologic processes accompanied by stasis, lateral intravenous urography can be done quite satisfactorily (Fig. 3A and B).



Fig. 2. Horizontal rotation with calyces directed posteriorly. Position of ureter and kidney otherwise normal. Constriction below ureteropelvic junction was shown on routine pyelogram. No surgery.

<sup>\*</sup> Read at the Thirty-ninth Annual Meeting, American Roentgen Ray Society, Atlantic City, N. J., Sept. 20-23, 1938.

#### NORMAL LATERAL PYELOGRAM

We usually, but with certain modification, use Mertz's criteria of the normal lateral pyelogram. The shadow of the pelvis is usually superimposed on that of the second lumbar vertebra, but sometimes on part of the first and second, or second and third lumbar vertebrae. The long axis of the renal pelvis and the spine correspond. The superior and inferior calyces extend up

convex posteriorly to deep in the pelvis where it again comes forward to enter the bladder (Figs. 1 and 2). The anterior surface of the ureter in relation to the peritoneum is fairly constant. Normal variables must be learned by experience.

#### ESSENTIAL INFORMATION

The lateral pyelogram should establish the type and the degree of rotation of the kidney, and the anteroposterior position of

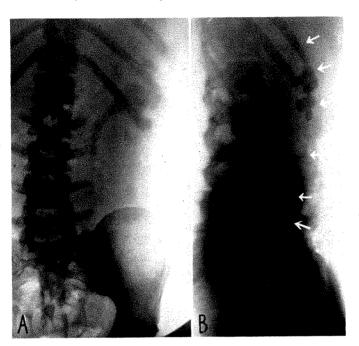


Fig. 3. A, sixty minute urogram. Kidney displaced laterally, more at upper pole. A dynamic type of hydronephrosis and hydroureter. Lumbar scoliosis with concavity to left, increased left-sided density, psoas muscle poorly visualized. Pathologic behavior of infection. B, anterior displacement of kidney and ureter. Slight vertical and horizontal rotation. Diagnosis of large perinephric abscess with generalized infection of retroperitoneal space made. Surgery: incision and drainage; 1,000 cc. pus obtained.

and down respectively (Fig. 1), but if there is some rotation of the kidney on its long axis, the significance of which is not yet entirely understood, the calyces may point backward towards the spinous processes, or be visualized through the pelvis (Fig. 2). The ureter descends in a smooth convex curve anteriorly behind the shadow of the vertebral bodies until it reaches the inferior margin of the fourth lumbar where it becomes anterior and passes downward just anterior to the fifth lumbar and the lumbosacral joint, then becomes slightly

the kidney and the ureter. We use Mertz's terminology of vertical and horizontal rotation, that is, rotation on the short and long axis respectively. Combination of types and degrees of rotation and displacement vary with different lesions and constitute the essential basis of diagnosis from lateral pyelography, but this information must be correlated with that obtained from the routine pyelogram, and pathologic behavior. The most significant combination is that of vertical rotation and displacement.

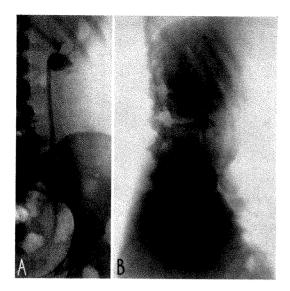


Fig. 4. A, large dense kidney, small hydronephrosis, moderately dilated ureter, apparently deformed lower calyces, lumbar scoliosis, concavity to left, increased left-sided tissue density becoming lateral and convex at brim of the pelvis. B, anterior displacement of the kidney and ureter, vertical rotation, lower pole forward. Perinephric abscess located inferiorly.

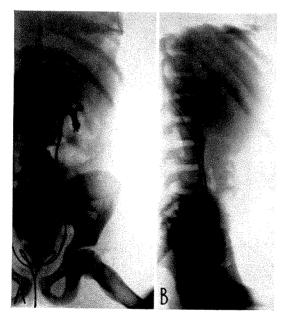


Fig. 5. 1, slight horizontal rotation. Spasm and irregular contraction of upper end of ureter. Small amount of gas in small bowel. B, slight anterior displacement of kidney and ureter, rotation chiefly horizontal. Roentgen diagnosis was perinephric infection but in addition there was a subcapsular abscess which was not diagnosed from roentgenogram.

#### LESIONS SUBJECT TO STUDY

We have found the information obtained helpful and at times conclusive in the diagnosis of the following lesions: renal neoplasms and cysts, perinephric abscess, primary retroperitoneal tumors, retroperitoneal infections, tumors arising from organs adjacent to kidney, retroperitoneal

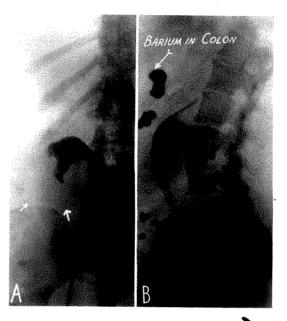


Fig. 6. A, enlarged lower renal pole (due to rotation). Questionable deformity of calyces. Clinical history suggested carcinoma of colon. Anteroposterior pyelograms showed what appeared to be a tumor of the kidney. B, kidney pelvis organically normal. Anterior displacement of kidney and ureter, vertical (short axis) and horizontal (long axis) rotation. Diagnosis: retroperitoneal tumor, probably sarcoma, slight mechanical hydronephrosis. Surgery and biopsy: chronic indurated perinephric abscess, normal kidney.

metastatic malignant growths, congenital and acquired abnormalities of the kidney and ureter, and in a large group of miscellaneous conditions encountered from time to time in the investigation of the urinary tract.

Perinephric Abscess. Since the retroperitoneal space is potential an increase in solid or fluid medium from inflammation manifests itself by extension along natural planes of tissue cleavage and by displacement of organs in the direction of least resistance which is usually forward and downward, modified occasionally by the difference in the relationship of the right and the left kidney.

Perinephric abscess causes predominantly anterior displacement of the kidney and the ureter, but this is associated with variable degrees of vertical and horizontal rotation (Figs. 3, 4 and 5). The amount of displacement depends upon the extent of the infiltration and the degree of suppuration (Fig. 3A and B), and the direction of rotation, the probable location of suppuration (Fig. 4A and B). When these dynamic signs are correlated with acute pathologic behavior, the diagnosis becomes relatively simple. A chronic indurated perinephric abscess without the evidence of acute pathologic behavior may be quite difficult, if not impossible, to differentiate from a retroperitoneal sarcoma (Fig. 6A and B). This simple procedure should decrease the number of explorations for acute abdomen, since perinephric abscess does cause considerable peritoneal irritation with symptoms easily mistaken for an intra-abdominal condition.

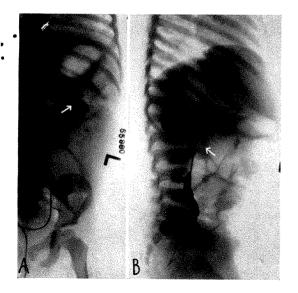


Fig. 7. A, horizontal rotation, outward displacement of the lower pole, filling defect in pelvis at tip of catheter. Information not conclusive. B, lateral roentgenogram shows invasion of pelvis. Working diagnosis of Wilms' tumor. Tumor regressed in size, and there was return of function following irradiation. (Courtesy of Dr. H. O. Mertz.)

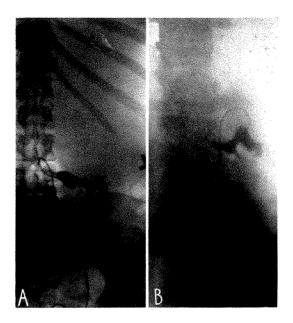


Fig. 8. A, large upper quadrant tumor. Kidney displaced to pelvic brim. Pelvis rotated. B, extreme vertical rotation, no appreciable anterior displacement, kidney pelvis intact. Sarcoma tail of pancreas. (Courtesy of Dr. H. O. Mertz.)

Tumors of the Kidney. The greater number of cortical neoplasms can be detected from the routine pyelogram. Occasionally, the lateral pyelogram will give the only conclusive evidence of a renal neoplasm (Fig. 7A and B), permit the differentiation of retroperitoneal tumors displacing the kidney (Fig. 8A and B), or prevent the diagnosis of tumor because of a vertically rotated kidney (Fig. 6A and B).

Cortical neoplasms cause predominantly vertical rotation, variable degrees of horizontal rotation, and little if any, more frequently no anterior displacement, of the kidney or the ureter, Mertz (Fig. 9B). If there is appreciable anterior displacement of the kidney and a localized segment of the ureter with evidence of an intrarenal malignant growth, the tumor has probably invaded perinephric structures and the choice between surgery and irradiation should be seriously considered because the case is probably inoperable (Fig. 10A and B). We suggest that the lateral pyelogram be employed in all cases clinically

or roentgenologically suspected of malignant growth.

Cysts. Large solitary cysts of the kidney cause considerable vertical and horizontal rotation without a comparable degree of anterior displacement, even when the cyst is huge (Figs. 11, 12 and 13), and most frequently there is no appreciable displacement (Figs. 12 and 13). Other criteria for

always a mechanical hydronephrosis which may be general or partial, due to chronic compensation which is more frequently not present in malignant neoplasms because of the more rapid growth of the latter. A great effort should be made to differentiate between small serous cysts and small neoplasms because the solitary cyst often causes no symptoms and a useless opera-

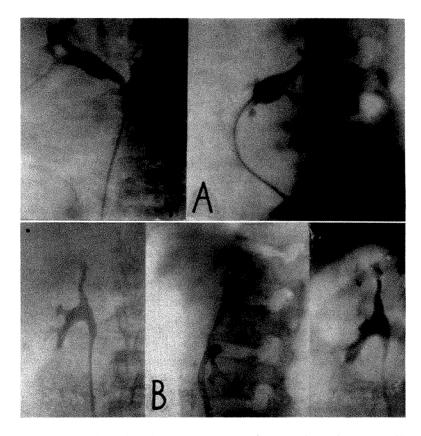


Fig. 9. A, anteroposterior and lateral pyelograms in a case of retroperitoneal sarcoma. There is considerable anterior displacement of the kidney and ureter and marked horizontal and vertical rotation of the kidney. B, the two small figures to the left show influence of hypernephroma. Vertical rotation of slight degree and compression of kidney pelvis. The single figure to extreme right, reading from left to right, shows increased size of the hypernephroma.

cysts must be employed. In our experience cysts cause less compression deformity than a malignant tumor of comparable size, rarely distort the pelvis unless there is associated infection, and often appear as an accessory rather than an incorporated mass because of the difference in the genesis of the lesion. There is practically

tion with clinical failure may be avoided. If there is an element of doubt the patient should receive the benefit of it. The differential diagnosis is particularly difficult when the small cyst involves the upper pole, because the law of probability favors a malignant neoplasm.

Retroperitoneal Tumors. These include

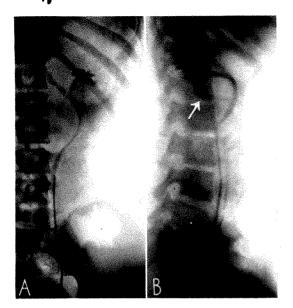


Fig. 10. A, calyces tuffed superiorly. Nonopaque filling defect in pelvis. Lateral displacement of kidney and upper end of ureter. Tumor of abnormally developed kidney suggested. Can the diagnosis be more specific? B, vertical and horizontal rotation; anterior displacement of kidney and upper end of ureter, lower half of kidney pelvis hydronephrotic and displaced upward; pathologic behavior of a malignant condition. Diagnosis of perinephric extension confirmed by surgery. Was not removable. No biopsy.

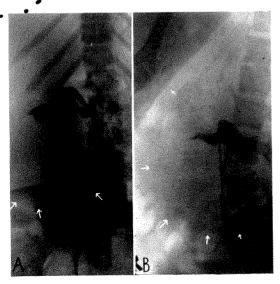


Fig. 12. A, large tumor lower pole of right kidney. Pelvis displaced upward and rotated. B, 90 degree vertical rotation lower calyces anteriorly. Hydronephrosis of cephalic calyces. No anterior displacement. Solitary cyst.

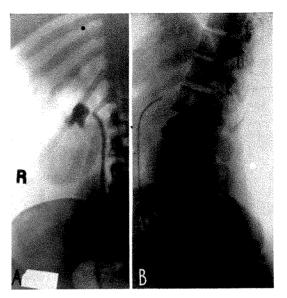


Fig. 11. A, large, slightly irregular tumor lower pole right kidney. Pelvis pushed up. Actual condition of pelvis not demonstrated. B, considerable vertical rotation of kidney, lower half of kidney pelvis compressed, but pelvis otherwise intact. No an terior displacement. Solitary cyst. (Courtesy of Dr. H. O. Mertz.)



Fig. 13. A, large tumor lower pole of left kidney displacing pelvis upward. Condition of pelvis not demonstrated. B, pelvis intact except for mild compression; 90 degree vertical rotation. No appreciable anterior displacement comparable to size of mass. Solitary cyst. (Courtesy of Dr. H. O. Mertz.)

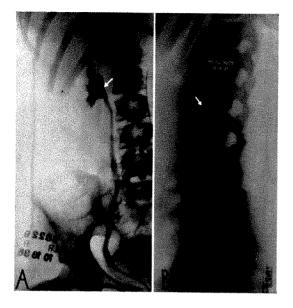


Fig. 14. A, appendectomy without relief. Urography: hydronephrosis from ureteropelvic junction obstruction. Retrograde: ureteropelvic junction obstruction evident but lesion is not demonstrated. B, lesion and sacculated hydronephrosis shown. Diagnosis of aberrant vessel. Is to return for surgery.

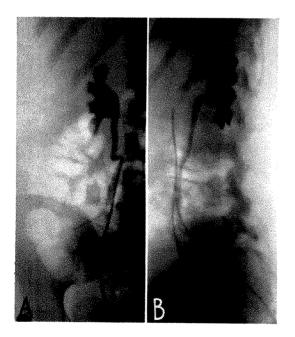


Fig. 15. A, anteroposterior roentgenogram fails to demonstrate exact type of ureteropelvic junction lesion but suggests aberrant vessel. Kinking at tip of catheter due to catheter. B, lateral roentgenogram shows unquestionable deformity of aberrant

both the true retroperitoneal sarcoma, and tumors originating from retroperitoneal organs other than kidney, particularly the tail of the pancreas. Primary retroperitoneal tumors cause considerable anterior displacement which is always associated with a considerable degree of horizontal

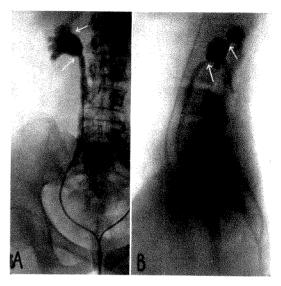


Fig. 16. A, stone demonstrated in pelvis by roent-genogram of the kidney, ureter and bladder included in medium and not visible on pyelogram. General, with localized increased hydronephrosis of upper calyx. Cause not clearly seen. B, stricture of cephalic infimidibulum causing increased partial hydronephrosis. Ureteropelvic junction obstruction causing general hydronephrosis. Evidence of infection which is more advanced in obstructed calyx. No surgery.

and vertical rotation (Figs. 8A and B and 9A), thus tending to differentiate them from perinephric abscess which causes predominantly anterior displacement of the kidney and ureter, and from primary renal tumors which cause predominantly vertical and horizontal rotation of the kidney without displacement or appreciable displacement of the kidney and the ureter. If a retroperitoneal lesion is demonstrated

vessel and the hydronephrosis to be larger, and sacculated. The kidney is a little posterior. A short pedicle was present. The possibility of a posterior position due to short pedicle will be studied in future cases.

and does not conform to these criteria one must carefully consider other possible origin with the probable result of the physical force of the lesion. This will at times determine its origin if not the actual nature of the tumor (Fig. 8A and B). The

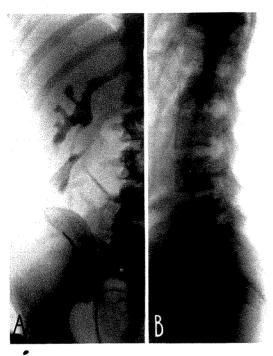


FIG. 17. A, crossed dystopia. Catheterization of right ureteral orifice failed to give relief. Catheterization of left ureteral orifice with relief. Urogram sixty minutes. Left catheter for drainage. Note correct point of direction of pelves and point of crossed kidney inferiorly. B, kidneys and ureters in relatively normal anteroposterior position.

lateral pyelogram thus emphasizes the importance of physical properties in urological diagnosis.

Miscellaneous. This includes too great a number of abnormal conditions to be discussed here. A good rule to follow is to make a lateral pyelogram when the routine pyelogram leaves one in doubt as to the probable significance of some aberration from the average normal. Congenital (Figs. 14 and 15) and acquired lesions (Fig. 16A and B) at the ureteropelvic junction, vague causes of partial and complete hydronephrosis (Fig. 15A and B), unusual appearing pelves (Figs. 4, 6, 7,

10, 11, 12 and 13), anomalies of development which might lead to clinical confusion (Fig. 17A and B), and calcifications anterior or posterior to the kidney which may appear to be in the kidney pelvis because of superimposition, and differentiation between intra-abdominal and retroperitoneal masses, etc., all lend themselves well to study by lateral pyelography.

#### SUMMARY

The lateral pyelogram has a wide range of usefulness. The technique is simple and does not appreciably delay the urologist or add to the discomfort of the patient. The normal variable is much less than in the average system which makes it relatively easy to detect the pathologic. It permits convincing localization between intra-abdominal and retroperitoneal tumors and in the differentiation of retroperitoneal lesions themselves, and can be used to advantage in the roentgenological investigation of all urinary tract problems. Elective lateral pyelography is of as much value as the lateralization of any other organ or system of organs and should be placed on an equal plane.

We wish to express our appreciation to the staff of the Kentucky Baptist Hospital for making this paper possible, and particularly to Drs. J. R. Stites and J. Andrew Bowen who have been more than generous in their helpful advice and in permitting the use of their urological material, and to Dr. H. O. Mertz, Indianapolis, Indiana, who has kindly contributed several illustrations.

#### REFERENCES

 MERTZ, H. O. The lateral pyelogram. J. Indiana M. Ass., 1931, 24, 537-541.

 Nichols, B. H., and Shiflett, E. L. Roentgenographic studies in diagnosis of renal tumors. *Med. Clin. North America*, 1934, 17, 1101–1123.

3. SHIFLETT, E. L. Correct diagnosis of the more common urologic lesions. *Radiology*, 1936, 26, 270–285.

SHIFLETT, E. L. Roentgen diagnosis of renal infections. Am. J. Roentgenol. & Rad. Therapy, 1939, 42, 689-692.

#### DISCUSSION

Dr. Bernard H. Nichols, Cleveland, Ohio. It was a pleasure to be asked to discuss

this paper because this is a subject which has apparently been somewhat neglected. As has been said, Dr. Mertz's paper on "Lateral Pyelography" showed the value and described definitely most of the occasions in which this method of examination may be utilized to advantage.

We have been much interested in lateral pyelography, particularly in the diagnosis and location of suspicious shadows in the region of the kidneys. Quite often it has been our experience that dense shadows which appeared to be calculi lost in the pyelographic medium on an anteroposterior exposure were, to our chagrin after making a pyelogram, shadows either posterior or anterior to the kidney. Therefore, we now almost routinely do a lateral pyelogram where renal calculi are suspected if they are not definitely identified by either a pyelogram or an excretory urogram.

We have also found this procedure to be a most valuable adjunct to our present methods of examination of patients suspected of having a perinephritic abscess. Dr Menville, in his paper on "Perinephritic Abscesses" published in the June issue of the Journal of the American Medical Association, described the importance of lateral pyelography as an aid in the diagnosis of these lesions. Dr. Shiflett, today, has again called attention to the value of this

procedure. It has been particularly valuable in cases of a well established abscess as, by the presence of the collection of pus at the lower pole of the kidney—usually the medial side the kidney is displaced forward, together with the ureter, which produces a somewhat crescent-shaped deformity. There are few things, except possibly a smooth, symmetrical tumor either of the lower pole of the kidney or a perirenal tumor and possibly an aneurysm of the abdominal aorta, which might produce such a deformity. However, with the clinical history and the other known findings which we have depended upon so long, it is not difficult in most instances to correctly establish the diagnosis of a perinephritic abscess.

With the present speculations that circulatory renal disturbance is a causative agent in the production of hypertension, lateral pyelograms, we feel, are of importance in determining the torsion of the kidney on its long axis. This may be a definite factor in circulatory disturbance if Dr. Goldblatt's findings are true, in which case this type of examination may become very valuable.

As the speaker has shown so well, there are many other uses for this type of examination and one in particular is the demonstration of a stricture of the upper end of the ureter in the presence of a redundancy.



## CALCULUS IN A URACHUS

## REPORT OF A CASE WITH ENURESIS\*

By GEORGE M. WYATT, M.D., and THOMAS H. LANMAN, M.D. BOSTON, MASSACHUSETTS

THE finding of a calculus in a urachus is unusual. A survey of the literature reveals only one reported case. In that instance, the stone was of considerable size, operation was refused, and the patient died of uremia.

The case reported below is of particular significance in that it again calls attention to the importance of giving the most careful consideration to the symptom of enuresis in a child. A variety of organic lesions in the urinary tract may be responsible for urinary incontinence in early life. Particularly important are certain congenital anomalies, among which are posterior urethral valves, ectopic ureters, anomalies of the spine, and lesions of the central nervous system.

Every effort must be made to exclude organic lesions before treating any patient with urinary incontinence as a mental or emotional problem.

#### REPORT OF CASE

The patient was a white male, aged seven, who came under our observation because of apparent inability to acquire normal urinary control. Bed wetting was constant. Control during the day was not normal, but on close questioning it was suggested that the lack of control was an urgency with incontinence rather than true incontinence.

His birth history and past history were entirely normal. He had had no serious illnesses. His parents were highly intelligent and had sought advice from several physicians regarding the boy's urinary difficulties, which were now causing considerable trouble, particularly because of comments by his school- and playmates. Repeated urinary analyses had failed to show any evidence of infection. General physical examination revealed no abnormalities.

Roentgenograms were taken of the lumbosacral spine in an effort to exclude a congenital anomaly of the spine as a causative factor in the enuresis. The calculus was noted on these films and described as being rather far anterior, but still within the limits of the bladder area. Intravenous pyelography was done to visualize the urinary tract and determine the exact location of the calculus in relation to the bladder (Fig. 1, A and B). The shadow of the calculus was seen to project anteriorly from the bladder wall in the region of the urachus. A diagnosis of stone in the lower end of the urachus was made and operation advised.

Operation. A midline suprapubic incision was made from just below the umbilicus to the symphysis. The rectus muscles were pulled laterally, the prevesical space entered, and the bladder freed. The peritoneum was stripped upward and on approaching the dome of the bladder, the fibrous cord of the urachus was seen. This cord-like structure fanned out as it entered the bladder wall. Incision was made just below it into the bladder and on exploring with the finger and everting the mucous membrane of the bladder a pedunculated mass the size of a large pea was encountered. This mass had its base in the bladder wall (Fig. 2). It was excised, and about 2 cm. of the tract of the urachus was excised with it. On cutting across this fibrous tract about 2 cm. distal to the bladder no lumen could be identified. The tract was tied at this point with catgut. A catheter was placed in the bladder. The bladder wall was closed about it in the usual manner. A drain was placed in the prevesical space and the skin and fascia closed with silk.

The pathologist's report is as follows:

Gross Description. The specimen consists of two pieces of tissue, one measuring 1.3×1.3×0.6 cm. in its greatest diameter, the other 1.1×0.5×0.3 cm. The first piece is roughly pearshaped, and reveals a normal appearing whitish-gray mucosal surface, except on one side where a recent cut surface of reddish color is noted. On palpation a firm stone-like mass is found in the center of this piece. The second specimen exhibits on one side a mucosal surface similar to that described above, while the other surfaces are of a reddish-yellow color. This

<sup>\*</sup> From the Departments of Roentgenology and Surgery of the Infants' Hospital, and the Children's Hospital, Boston, Massachusetts.

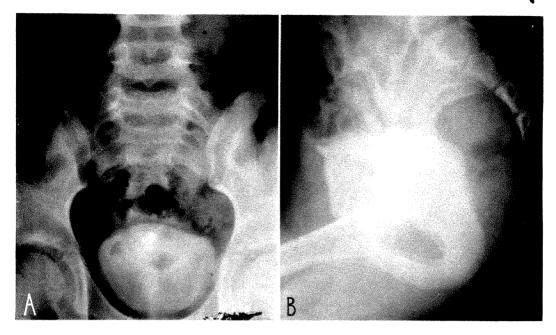


Fig. 1. A, anteroposterior film of the urinary tract following intravenous injection of 17 cc. of 35 per cent diodrast shows the shadow of the calculus to lie within the margins of the dye-filled bladder. B, in the lateral view, the shadow of the calculus projects anteriorly from the margin of the bladder in the region of the urachus.

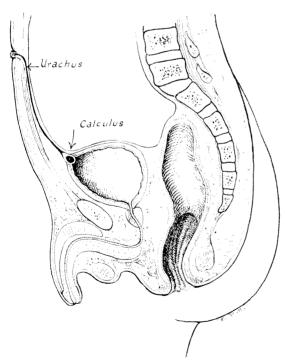


Fig. 2. Diagrammatic sagittal section through the lower abdomen shows the relationship of the urachal remnant and the calculus to the abdominal wall and bladder.



Fig. 3. Photomicrograph of a section through the calculus. A, area of calcification; B, bone; C, connective tissue.

piece is of tendon-like consistency. No lumen is found in the specimen. Representative sections are placed in Zenker's fluid and 10 per cent formalin.

Microscopic. Three sections stained with eosin, methylene blue were examined. The sections show connective tissue which in one section is covered by a lining of transitional epithelium. The connective tissue immediately below this transitional epithelium is loose and contains numerous congested vessels and numerous small areas of recent hemorrhage. In another section the connective tissue is of a more dense collagenous character, and intermingled with numerous bundles of smooth muscle fibers. The third section shows the connective tissue which surrounds and includes large deposits of calcium and some newly formed bone.

This area of calcification, which is completely surrounded by dense connective tissue, consists of numerous small and large masses of dense basic staining material, often arranged in circular masses. Scattered throughout the area of calcification are small masses exhibiting definite bone formation. Nuclear structures stain poorly and osteoblastic activity is not marked (Fig. 3).

Diagnosis. Calcification and ossification of remnant of urachal cyst.

The patient had an uninterrupted convalescence and was discharged on the sixteenth postoperative day, at which time the suprapubic wound had healed, and he was voiding normally through the urethra.

It is gratifying to report that since operation the boy's control during the day became practically normal within a very short time. The night bed wetting was a little harder to overcome, but now, four months after operation, the parents report that he has no trouble except occasionally when he is overtired. These episodes are becoming less and less frequent.

#### DISCUSSION

It is interesting to speculate on the reason for the enuresis. The mass in the bladder wall probably interfered with the neuromuscular mechanism of the bladder sphincter. While it could not be compared with the urgency due to a badly infected bladder with a loose stone, it is reasonable to assume that this mass did have a certain amount of mobility which contributed to the disturbed function. This conclusion is supported by the clinical improvement of the patient following removal of the calculus.

#### REFERENCES

- CAMPBELL, MEREDITH F. Pediatric Urology. The Macmillan Co., New York, 1937, Vol. I, p. 298.
- 2. Lanman, T. H., and Moore, J. H, Surgical significance of urinary incontinence in infants and children. New England. J. Med., 1938, 219, 777–782.



# PULMONARY LESIONS AFTER ROENTGEN AND RADIUM IRRADIATION\*

By ROLF BULL ENGELSTAD

From the Norwegian Radium Hospital Oslo, NORWAY

IN PREVIOUS papers I have reported on experimental investigations proving that roentgen irradiation produces very marked lesions of the lungs in rabbits.† These lesions are degenerative and inflammatory changes of varying degree, followed by regenerative changes. The lung reaction has a characteristic development, in which four stages can be distinguished:

Stage 1. The initial stage, commencing one to two hours after the irradiation and lasting one to two days. Here we find degeneration of the lymph follicles, changes in the bronchial epithelium with abundant mucus secretion, hyperemia, increased transudation and moderate leukocytic infiltration.

Stage 2. The latent stage, with a duration of two or three weeks.

Stage 3. The main reaction, with marked degenerative and inflammatory changes. The inflammation may be more or less acute, after very large doses often fulminant. The acute inflammation has its maximum one to two months after the irradiation. Subsequently the leukocytic infiltration slowly diminishes and we then find large quantities of macrophages and often a great number of giant cells.

Stage 4. A stage with principally regenerative changes, with proliferation of connective tissue and sclerosis, bone production is not uncommon, and there is a slight proliferation of the bronchial epithelium.

With regard to the radiosensitivity of the lungs of the rabbits I have found:

- 1. After subepidermicidal doses the lung changes, as a rule, are slight and of short duration.
- 2. After epidermicidal doses the altera-

- tions are very pronounced and leave a marked sclerosis, often with bone production.
- 3. After still larger, dangerous or lethal doses the lung reaction is exceedingly strong and very often has a fatal outcome.

In view of these experiences it is reasonable to assume that after large roentgen and radium doses lesions of the human lungs will also be found, and in fact, not a few of such cases are reported in the literature, especially in that of the years immediately after the introduction of deep roentgen therapy.

In our own material I have so far found 36 cases which have been interpreted as pulmonary lesions due to roentgen or radium irradiation. I must, however, here and now emphasize that it is very difficult to make an absolutely certain diagnosis of these lesions. In order to make the diagnosis as certain as possible a roentgenogram must be taken before the treatment and it is necessary to watch the patient for several months afterwards, with repeated roentgen examinations.

The clinical symptoms are not very characteristic. During the treatment, or a short time afterwards, the patient develops a cough, which can be very annoying, and sometimes also fever. Pains in the chest are not common. The physical examination does not usually reveal any pathological changes, and it is only in a few cases that signs of pulmonary infiltration are found.

The findings at the roentgen examination vary. Most commonly irregular spotted or striped shadows are seen, in some cases also a more diffuse infiltration. The

<sup>\*</sup> Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13-17, 1937.

<sup>†</sup> Engelstad, R. B. Ueber die Wirkungen der Röntgenstrahlen auf die Lungen. Acta radiol., suppl. 19, 1934, pp. 1-94.

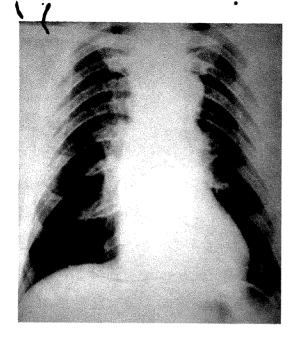


Fig. 1. Case 1. Male, aged sixty-six, carcinoma of the esophagus. Before treatment.

shadow stripes may have a fan-shaped arrangement, radiating from the hilum into the lungs. The roentgen picture may, in other cases, be mistaken for pulmonary metastasis. After some weeks these changes begin to diminish little by little, and in a

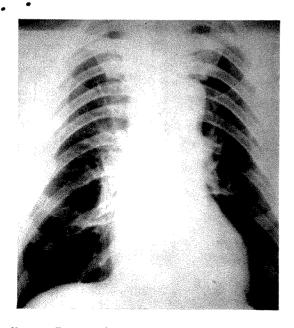


Fig. 2. Case 1. After roentgen treatment over four fields, total dose 8,240 r, daily dose 100-200 r.

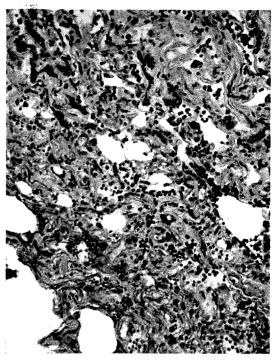


Fig. 3. Case 1. Showing hyperemia, edema, lymphocytic and leukocytic infiltration.

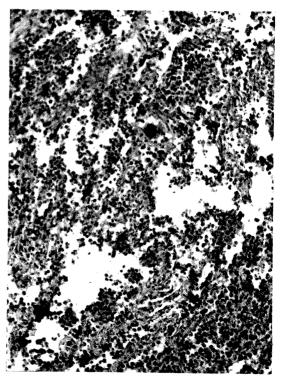


Fig. 4. Case 1. Showing lymphocytic infiltration.

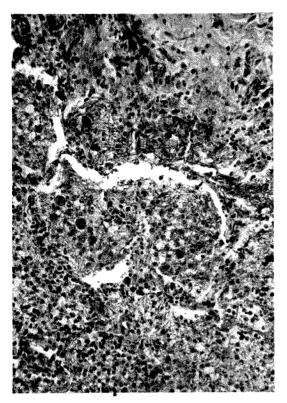


Fig. 5. Case 1. Showing lymphocytic infiltration and macrophages.

few cases they disappear completely. As a rule, however, sharply outlined spots and

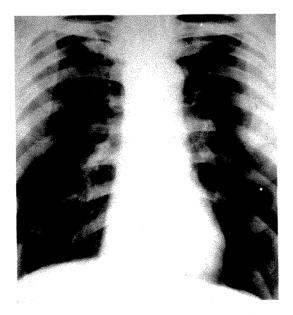


Fig. 6. Case II. Male, aged sixty-seven, carcinoma of the esophagus. Before treatment.

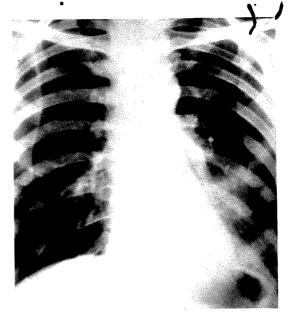


Fig. 7. Case II. After roentgen treatment over two fields, total dose 4,600 r, daily dose 200 r.

stripes are found in the late stages, as a result of the fibrous changes following the reaction. Retraction of the irradiated side may be seen. Thus, the roentgen findings do not differ in any characteristic manner from those in other inflammatory diseases of the lungs. The diagnosis of the radiation lesions of the lungs can therefore only be •

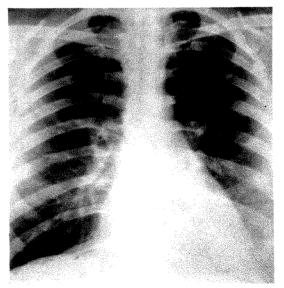


Fig. 8. Case III. Female, aged forty-eight, carcinoma of both breasts. Before treatment.

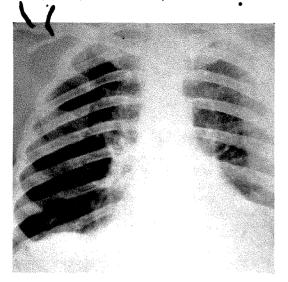


Fig. 9. Case 111. After radium treatment (three years, several series). Dose: 36+55+36+6+42+41+37+30+30 Dominici units.

made after protracted observation of the patient.

In most of our cases the clinical and roentgenological symptoms have been moderate, but we have also seen very pronounced reactions. It is impossible here to give a detailed description of all of our cases; I will therefore confine myself to demonstrating some typical examples.

Case 1. Male, aged sixty-six, with esophageal carcinoma. Roentgen treatment over four fields,

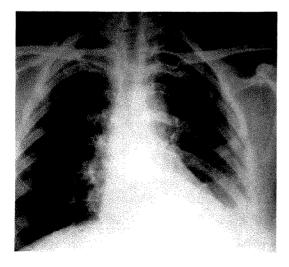


Fig. 10. Case IV. Female, aged fifty, carcinoma of right breast. Before treatment.

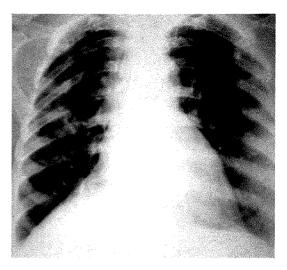


Fig. 11. Case IV. After roentgen treatment, total dose 3,420 r, and radium treatment, total dose 46+30 Dominici units.

total dose 8,240 r, daily dose 100–200 r. Before the treatment no pathological changes in the lungs. After the treatment signs of pulmonary infiltration, partly as a homogeneous slight shadow, partly as a more irregular infiltrative process. The patient died marasmic three months after the treatment. In the irradiated parts of the lungs the microscopical examination revealed foci of a marked fibrosis and of leukocytic and lymphocytic infiltration as well as large quantities of macrophages (Figs. 1–5).

Case II. Male, aged sixty-seven, with esophageal carcinoma. Roentgen treatment over

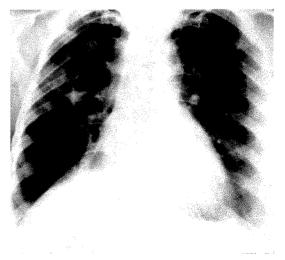


Fig. 12. Case IV. Eight months after treatment.

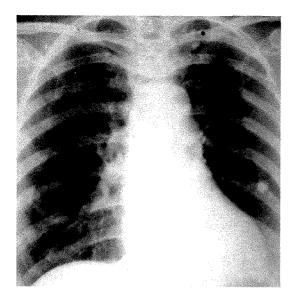


Fig. 13. Case v. Female, aged fifty-eight, recurrence after operation for carcinoma of the right breast, Before treatment.

two fields, total dose 4,600 r, daily dose 200 r. Roentgen examination before the treatment: a calcified focus in the right lung, but no other pathological changes in the lungs. After the treatment a widespread infiltration was found in the lower part of the left lung (Figs. 6 and 7).

CASE III. Female, aged forty-eight, with carcinoma of both breasts. She was given during

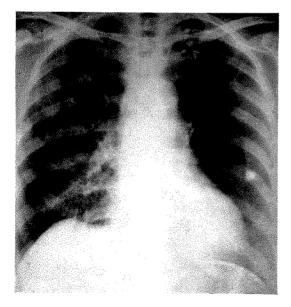


Fig. 14. Case v. After teleradium treatment with large doses.

the course of three years several series of adium treatment with very large total doses (36+55+36+6+42+41+37+30+30) Dominici units). Roentgen examination before the treatment: normal lungs. After the treatment: infiltration in both lungs, especially in the left (Figs. 8 and 9).

MAY, 1010

CASE IV. Female, aged fifty, with carcinoma of the right breast. Treated with roentgen rays, total dose 3,420 r, and with radium 46+30 Dominici units. Roentgen examination before the treatment: a calcified focus in the right lung, but no other pathological changes. After the treatment: a conglomeration of infiltrations,

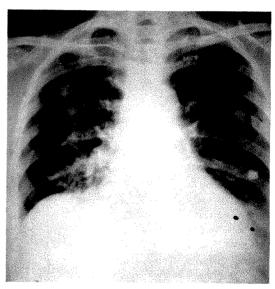


Fig. 15. Case v. Six months after treatment.

increasing in size during the immediately succeeding months and then diminishing, leaving a dense, sharply outlined, star-like infiltration (Figs. 10, 11 and 12).

Case v. Female, aged fifty-eight, with carcinoma of the right breast. She was operated upon, had recurrences and was treated with teleradium at another hospital. Roentgen examination before the treatment: a calcified focus in the left lung, but no other pulmonary infiltration. After the treatment: a widespread infiltrative process in the right lung with a network of shadow stripes. Some months afterwards the infiltration began to diminish and was followed by a pronounced fibrosis with shrinking of the lung (Figs. 13, 14 and 15).

36 patients having a demonstrable lung reaction, were treated for the following tumors:

	Cases
Carcinoma of the breast	21
Carcinoma of the esophagus	10
Pulmonary metastasis from extrapulmonary	
primary tumors	4
Primary carcinoma of the lung	1

During the same period of time 386 cases of breast carcinoma and 49 cases of esophageal carcinoma have been treated. The frequency of the radiation reaction in the lungs is thus:

Carcinoma of the	breast	5.4%
Carcinoma of the	esophagus	20.4%

All the patients with esophageal carcinoma have had roentgen treatment, mostly over four fields and usually with a total dose of 8,000-10,000 r. Most of them have also been treated with radium in a sound in the esophagus.

In the cases of breast carcinoma the treatment has been:

	Cases
Roentgen treatment	5
Radiumetreatment	11
Roentgen and radium treatment	5

The radium treatment was in some cases given as a teleradium treatment, the radium-skin distance being 5-6 cm., but in most cases with radium on a mould, the distance being 3 cm. Usually an epider-

micidal dose was given. When roentgen treatment was used, it was always given as a tangential irradiation.

The pulmonary tumors were all treated with roentgen rays. The roentgen treatment was in these, as in all the other cases, prolonged and fractionated, with daily doses of 100-200 r and a total dose up to 13,000 r, the number of fields varying from two to six.

The conclusion that can be drawn from this investigation is that in irradiation of the thorax, in mammary carcinoma, esophageal carcinoma, mediastinal and pulmonary tumors, one must count on the possibility of a pulmonary lesion caused by the roentgen or gamma rays, particularly when several fields are irradiated and an epidermicidal dose is given. After small doses pulmonary lesions are not seen. In our material very large doses of roentgen or gamma rays have been used in almost all the cases where a radiation reaction was demonstrated in the lungs.

The radiosensitivity of the human lung seems to correspond rather well with that of the rabbit. The histological findings also seem to be similar to those in rabbits.

The subjective, physical and roentgenological symptoms are not very characteristic and a prolonged period of observation is necessary in order to make the diagnosis. Pulmonary injuries with fatal outcome due to irradiation have in our material not been observed.



## RADIATION REACTION IN THE LUNG\*



By SHIELDS WARREN, M.D., and JACK SPENCER, M.D. BOSTON, MASSACHUSETTS

#### INTRODUCTION

WHILE it was noted as long as forty years ago by Bergonié and Tessier<sup>1</sup> that intensive irradiation of the thorax could produce an inflammatory reaction in the lung, and scattered clinical and experimental observations have been made since, there has been but little progress in our understanding of this field. In fact, until recently, many radiologists have been inclined to regard with skepticism the existence of pulmonic changes resulting from therapeutic irradiation.

The first series of experiments primarily focused on the effect of radiation on the lungs was carried out by Wohlauer<sup>19</sup> on 10 guinea pigs. They received doses ranging from 7.5 times the dose required to produce dermatitis to a fraction of that dose. He regarded pulmonary hyperemia and recent and old hemorrhages as evidences of radiation effect. In addition, there was slight leukocytic exudation into the alveoli in some of the animals as well as some dilatation of the perivascular and peribronchial lymphatics, which he regarded as probably secondary to the congestion. He interpreted the absence of alteration in the alveolar lining cells as an indication of their refractoriness to roentgen rays.

Early studies were focused on the effect of radiation on pulmonary tuberculosis rather than on the lungs themselves. A series of experiments by Küpferle<sup>11</sup> and others from 1912 on brought out the fact that there was more fibrosis adjacent to the tuberculous process in the irradiated animals than in the controls. The amount of radiation and the time consumed in giving it varied considerably.

In the course of a series of experiments on the effect of radiation on the gastro-intestinal tract, Warren and Whipple<sup>16</sup>

exposed the thoraxes of 3 dogs to medium wave roentgen rays in amounts from 350 to 450 ma-min. There was no clinical or postmortem evidence of pulmonary damage, although there were marked changes in the gastrointestinal tract.

Hines9 was the first to recognize radiation reaction of the lungs in his report of autopsy findings in 2 cases of supposed radiation reaction of the lung in 1922. The microscopic lung changes in the first case are of uncertain character, being complicated by widespread pulmonary metastases from a sarcoma of the arm. The patient, a male aged forty-six, received approximately 5,000 ma-min. at 140 kv., 20 inch distance, with a filter of I mm. copper and I mm. aluminum and 2,400 ma-min. at 125 kv., 12 inch distance, with a filter of 10 mm. aluminum. The right lung, weighing 1,100 grams, showed dense pleural adhesions which were absent from the left. The left, weighing 1,000 grams, was described as dry, tough, and brown. Both lungs contained numerous metastases. Aside from widespread tumor infiltration, microscopic examination showed obliteration of many alveoli by fibrosis of their walls and hyperplasia of the perivascular and peribronchial connective tissue. The author also mentions edema of alveoli and some epithelial desquamation. changes may occur in many different conditions and in this case the sequence of cause and effect is not clearly demonstrated. It is our opinion that the changes described in his second case may be due to metastatic malignancy rather than to the very small amount of radiation which was given.

Groover, Christie and Merritt<sup>8</sup> reported the clinical and roentgenographic findings in one case of pleuropneumonitis ending

<sup>\*</sup> From the Collis P. Huntington, New England Deaconess, and Pondville Hospitals, and the Department of Pathology, Harvard Medical School, Boston.

in cinical evidence of fibrosis following roentgen therapy of the chest for mammary cancer. They mention but do not describe transient changes in other cases. Cough, respiratory embarrassment, and increased roentgenographic density of the lungs developing at about the height of the cutaneous reaction and subsiding in six to eight weeks were noted following treatment with roentgen rays generated at 8.5 to 9.5 inch spark gap, 12 inch focal skin distance, and filtration through 0.5 mm. copper and 1 mm. aluminum in each field.

Wintz<sup>18</sup> pointed out that irradiation of mammary and pulmonary cancer particularly tends to produce pulmonary change. Evans and Leucutia<sup>5</sup> showed that lung changes are dependent on the quantity of radiation rather than on its wave length. One case of clinical radiation pneumonitis and 2 autopsies of irradiated chest cases which showed thickening of alveolar walls were reported by Fike.<sup>6</sup>

Desjardins,<sup>2</sup> in his review of the effect of radiation on the heart and respiratory system, mentioned that he had seen some degree of pleuropneumonitis in "about 2.5 per cent of several hundred patients, in which the thorax was irradiated for 40 or 45 minutes (800 r to 1000 r in air), but has never seen such reaction after exposure for 30 minutes (600 r in air), even when repeated several times at intervals of three or four weeks."

In 1934 a group of 4 cases of pulmonary radiation reaction, only one of which came to autopsy, was reported by McIntosh<sup>12</sup> together with 4 other probable cases. In the one autopsied case, an inoperable carcinoma of the breast was treated with over 10,000 r at 200 kv. The size of the portals was not reported. About ten weeks after the first treatment a cough developed. After three months, additional radiation was given and ten days later the patient developed a fatal bronchopneumonia. The lungs showed thickened pleurae with fibrinopurulent pleuritis. The lung parenchyma showed consolidation with dense, patchy, dull white foci, many in relation

to the smaller bronchi. Definite peribronchial fibrosis was present. Microscopic sections showed thickening of the alveolar walls, some exfoliation of the lining cells and perivascular and peribronchial thickening in all sections. The nature of the "thickening" was not specified. Widespread pneumonia was also present.

Transient radiation changes were detected by clinical and roentgenographic means by Downs<sup>3</sup> in 11 out of 53 cases of carcinoma of the breast in which the chest had been irradiated. There were no postmortem observations. Seven of the cases had received more than 7,000 r and 4 cases more than 10,000 r. The changes were transient in all but one case, a female aged sixty-nine, who had had radium needles implanted in the axilla.

Engelstad<sup>4</sup> reported lung changes interpreted as resulting from radiation in 21 (5.4 per cent) of 386 cases of irradiated breast carcinoma and in 10 (20.4 per cent) of 49 cases irradiated for carcinoma of the esophagus. Cases of radiation reaction followed large dosages, some from 6,400–13,000 r. One of the described cases was autopsied.

While clinical and roentgenologic pulmonary changes have been reported following heavy external irradiation in various cases (Hsieh and Kimm<sup>10</sup> among others), supporting pathologic observations are few or absent.

Most of the observed cases have been associated with radiation treatment of carcinoma of the breast. Thirty-six such cases were found by McIntosh and Spitz<sup>13</sup> among 60 followed clinically and roentgenologically. Autopsies were obtained in 6 cases, as well as one additional case due to irradiation of chest metastases in a child five years of age. The pathologic findings, though briefly reported, are in accord with those usually described: "Histologically the alveolar walls were generally thickened; the alveolar epithelium was desquamated into the air vesicles. Definite increase of perivascular and peribronchial connective tissue was present.

The bronchial lymph nodes were hemorrhagic and in places necrotie. Scattered lymphocytes were found throughout." Fifteen of the cases were severe, as judged from the films, and two-thirds of these showed symptoms two to six months after treatment. The milder grades of radiation pneumonitis were symptomless. One fatal case has been reported by Rajewsky<sup>14</sup>, a twenty-four year old worker in a radium plant, who was exposed for three years and died after two years of dyspnea and weakness. His lungs showed "diffuse induration, with spots of fibrous hepatization and carnification."

While some radiologists have recognized the roentgenological picture and clinical symptoms of pulmonary changes subsequent to irradiation as forming a fairly distinct entity, little definite evidence has accumulated as to the factors which determine the onset, permanence, and duration of radiation pneumonitis. The rare postmortem observations on these cases are disappointing and reveal only vague changes, chiefly of a chronic nature, which seem to obscure still more rather than to illuminate the process. But all these observations seem to have established beyond doubt the fact that the lung, like other tissues—as skin or mucous membrane —often suffers from residual changes following treatment with radium or roentgen rays which may be prejudicial to the patient's health. Clinical evidence points to two types of changes, one transitory and the other permanent. Since the pathology of these changes has received little attention, it seemed worth while, in view of the ever increasing use of radiation therapy, to attempt to define more exactly their nature and incidence.

#### FRESENT STUDY

Our method of procedure has been, first, selection, on a histologic basis, from our autopsy series, of the lungs which showed changes which we considered due to irradiation; second, verification of these by history; third, correlation of his-

tologic, gross, clinical, and radiation ctors in these cases; and finally, reconstruction of the sequence of histologic changes of radiation pneumonitis.\* Complete records of typical cases will be appended.

The pulmonary alterations which first attracted our attention occurred in a case (Case III) in which, although the amount of radiation given was not great, the changes could only be interpreted as due to radiation. This case will be presented in detail later. It must be borne in mind in discussion of the histologic changes following irradiation that unique histologic reactions are almost unknown. It is chiefly through typical combinations of cellular changes or the presence of the causative agent, as amoeba, spirochete, bacillus, etc., that the pathologist recognizes and classifies disease processes. The salient points which we have used in differentiating radiation reaction from other inflammatory changes in lungs are: (1) a hyali... membrane closely adherent to alveolar walls and never present alone but always associated with one or all of the following changes: (2) swollen alveolar lining cells either with or without desquamation and fibrosis, edema, or mild inflammatory exudation in the supporting tissue; (3)edema without appreciable inflammatory reaction; (4) diffuse alveolar fibrosis without evidence of organizing pneumonia, tuberculosis or silicosis; (5) an unusual fibrillar hyalinization of alveolar walls; (6) hyalinization of arterial walls; (7) interalveolar capillary changes such as swelling of endothelium and thrombosis. All of these changes are frequently seen in one section, but there is great variability in their degree and extent. These criteria and their relative values will be discussed later.

We have reviewed all the cases (398) with tumors situated between the diaphragm and the neck coming to autopsy in the Huntington, Deaconess, and Pondville Hospitals. The lung slides on these 398 cases were reviewed and classified on the

<sup>\*</sup>By pneumonitis we mean an inflammatory response involving the parenchyma of the lung and not restricted to the alveoli.

base of the histologic picture presented, using the above changes as guides, into three groups—positive, suggestive, negative—according to whether the changes present were considered referable to irradiation. Throughout this discussion it is important to keep in mind the nature of our material. The sections were often taken without reference to lobes. In many of the cases there was little lung tissue which was not involved by tumor. Samples taken without reference to the irradiated field may be inadequate for such a study as this.

The autopsy protocols, histories, and roentgenograms of these cases were then studied. In this group, 234 of the cases had received some irradiation over the thorax and 163 had not received any type of irradiation which could possibly affect the lungs. The irradiated cases had received from 15,000 to 800 r; a few of the cases of breast cancer had been treated by implantation of radium needles only. To our surprise only 3 of the 31 cases which we had classified on a purely empirical basis as radiation pneumonitis had not been irradiated. This gave greater confidence in our criteria in view of the fact that there were many cases of aspiration pneumonia and chronic pneumonitis in the group which might be supposed to confuse the picture. The relation of the presence of reaction to the amount of radiation will be discussed later.

While the gross observations as described in the protocols were often unsatisfactory and difficult to evaluate, none the less, certain significant changes were occasionally described. Most important was a dry, rubbery texture, the lungs being noncrepitant or only slightly crepitant, and tending to be pale with a suggestion of diffuse fibrosis. In some of our cases pleural fibrosis was absent, and in none could its existence be ascribed to irradiation alone. Pleural fibrosis is induced by so many agents that a causal relationship to irradiation is difficult to establish with certainty in any given patient. A few of the lungs

were slightly edematous and congested, suggesting interstitial pneumonitis.

In most cases adequate, and in many detailed, histories were available. From this standpoint, a nonproductive cough was the most important symptom, although dyspnea and chest pain were also significant indications of pulmonary changes. In this respect our findings coincide with those so adequately described in the literature.

Evidence of lung changes based on a study of roentgenograms of the chest was less satisfactory, since only 62 of the 163 cases had had chest films taken two months or more after therapeutic irradiation. In 53 other cases of this group post-irradiation chest films were taken at such short intervals after irradiation as to be inconclusive. In 36 of the 62 cases the presence of bronchopneumonia, metastatic tumor, or fluid so masked the picture as to render the determination of radiation changes impossible. Five cases (8 per cent) showed evidences of radiation reaction-pleuropulmonitis, progressive fibrosis of the irradiated lung field, or traction of the mediastinum.

The amount of radiation, symptomatology, and pulmonic change are correlated in the tables. In these tables we see that the cases are restricted to a relatively small group, the breast carcinomas naturally predominating because of the greater frequency of thoracic irradiation in this relatively common type of neoplasm. Since roentgen therapy to bronchial and esophageal neoplasms can only be achieved by traversing at least a part of the lung, these cases also frequently show radiation reaction.

In correlating these factors it became apparent that acute, late, and combined acute and late types of reaction could be recognized. The time intervals during treatment and from irradiation to death in large part determined the type of reaction found on postmortem examination, explaining the absence of reaction in some cases which had received large amounts of radiation.

Lung

### Shields Warren and Jack Spencer



# $T_{\rm ABLE~I}$ cases showing pulmonary radiation reactions

## A. Acute Reactions a. Definite

Case	Location				Treatm	ents			Interval between	Interval from Last
No.	of Tumor	Age	Sex	Date	Amount	Total Amount	Portals	kv.	First and Last Series of Irradia- tion	Irradia- tion to Death
I	Breast	58	Ŷ	Oct. 1936 Dec. 1936 Jan. 1937	I,200 r 2,800 r 600 r I,800 r	6,400 r	Large Small Small	400	12 weeks	16 weeks
11	Breast	52	Q	Apr. 1930 Oct. 1930	3,200 r 1,600 r	4,800 r	Large	180	22 weeks	8 weeks
111	Mediasti- num	56	Ŷ	Oct. 1936 Dec. 1936 Feb. 1937	I,200 r I,200 r I20 r	2,520 r	Large	200	20 weeks	ı day
IV	Breast	86	Q.	Sept. 1934	600 r	600 r	Large	200		6 days
	•			ь.	Suggestive	2				
v	Esophagus	79	♂	Jan.–Feb. 1932	3,000 r	3,000 r	Large	200	4 weeks	10 days
VI	Esophagus	53	♂	Dec. 1933	3,600 r	3,600 r	Small	200	4 weeks	2 weeks
VII	Breast	45	ę	May 1934 June 1934	I ,200 r 17 ,320 mg-hr.		Large	180	4 weeks	12 weeks
VIII	Breast	47	Q	AugSept. 1933	1,800 r	1,800 r	Large	200	3 weeks	52 weeks
							-			

### B. Acute and Late Radiation Reactions

Aug.—Sept. 1937 | 1,200 r | 1,200 r | Small | 200

3 weeks

4 weeks

### a. Definite

Case	Location				Treatm	ents			Interval between First and	Interval from Last
No.	of Tumor	Age	Sex	Date	Amount	Total Amount	Portals	kv.	Last Series	Irradia-
х	Breast	55	P	May–June 1936 Nov.–Dec. 1936– Jan. 1937	3,800 r 2,600 r	6,400 r	Large	200	32 weeks	3 days
XI	Breast	50	Q	SeptOct. 1936	3,600 r	3,600 r	Large	180	4 weeks	8 weeks

### Radiation Reaction in the Lung

### TABLE I (Cont.)

### B. Acute and Late Radiation Reactions (Cont.)

### a. Definite (Cont.)

·	1				Treatm	ents			Interval between First and	Interval from Last
Case No.	Location of Tumor	Age	Sex	Date	Amount	Total Amount	Portals	kv.	Last Series of Irradia- tion	Irradia- tion to Death
XII	Breast	54	P	Dec. 1930 Jan. 1931 May 1931	I,400 r 2,000 r I,200 r	4,600 r	Large	200	35 weeks	8 weeks
XIII	Breast	39	Ŷ	Dec. 1931- Nov. 1932	8,000*- 9,000 r		Large	180	52 weeks	1 week
XIV	Esophagus	70	♂	Feb.–Mar. 1937 May 1937	6,400 r 1,800 r	8,200 r	Small	200	11 weeks	4 weeks
xv	Breast	43	Ŷ	July-Oct. 1931 AprJuly 1932 Dec. 1932 FebMar. 1933	3,200 r 1,600 r 800 r 800 r	6,400 r	Large	180	84 weeks	12 weeks
XVI	Breast	62	♂	Dec. 1935– May 1936 Aug. 1936 Oct. 1936	7,000 r 3,600 r 2,400 r	13,000 r	Large	200	• 39 weeks	9 weeks
XVII	Bronchus	61	♂	Mar. 1936 Apr. 1936	1,600 r 900 r	2,500 r	Large	200	2 weeks	5 weeks
XVIII	Breast	41	ę	Nov. 1927 May 1928 July 1932	600 r 600 r 1,000 r	2,200 r	Large	170	230 weeks	2½ years
xıx†	Breast	52	Q	May-July 1937	7,900 r	7,900 r	Large and small	1,000	8 weeks	26 weeks

### b. Suggestive

XX	Mediasti- num Breast	35	Ŷ	FebMar. 1931	15,000*- 16,000 r		Large	180	108 weeks	8 weeks
XXI	Bronchus	68	♂	Apr. 1934 June 1934	4,000 r 4,000 r	8,000 r	Small	180	11 weeks	12 weeks
XXII	Breast	55	φ	Apr. 1935 June 1935 Sept. 1935	3,600 r 1,600 r 2,100 r	7,300 r	Large Small Small	180	12 weeks	29 weeks

<sup>\*</sup> This represents approximate amount. Exact amount not known, as much of treatment was received in other hospitals. † This case was first observed clinically. It is not one of the group of 398 cases studied primarily from the histologic angle.

### Shields Warren and Jack Spencer

### TABLE I (Cont.)

### B. Acute and Late Radiation Reactions (Cont.)

b. Suggestive (Cont.)

Case No.	Location					Interval between First and	Interval from Last			
	of Tumor	Age	Sex	Date	Amount	Total Amount	Portals	kv.	Last Series of Irradia- tion	Irradia- tion to Death
	D			MarMay 1928	3,000 r	4,200 r	and			
XXIII†	Breast	59	9	NovDec. 1928	I,200 r		small	200	34 weeks	20 weeks
XXIV	Breast	49	φ	July 1935 Aug. 1935	1,200 r 500 r	I,700 r	Large	180	4 weeks	16 weeks

<sup>\*</sup> This represents approximate amount. Exact amount not known, as much of treatment was received in other hospitals. † Lead therapy also.

### C. Late Radiation Reactions

### a. Definite

XXV	Breast	• 57	φ	Oct. 1931 Jan. 1932 Mar. 1932 May-Nov. 1934 MarApr. 1936	600 r 1,800 r 3,400 r	10,000 r	Large	200 200 200	96 weeks	12 weeks
XXV	Breast	• 57	Q	Mar. 1931 1,5	4,800 r 1,200 r					

### b. Suggestive

XXVII	Breast	66	ę	Nov. 1934 Jan. 1935 Aug. 1935 July 1936 Feb. 1937	300 r 1,500 r 1,200 r 600 r 1,200 r	4,800 r	Large	200	116 weeks	18 weeks
XXVIII	Breast	53	Q	July 1936	23,112 mg-hr. radium	į			_	1 week
XXIX	Breast	64	P	May 1932 June 1932	1,200 r 600 r	1,800 r	Large	200	3 weeks	52 weeks

It must be remembered that the time intervals implied in the terms "acute" and "late" are different from those in common usage. As in other types of radiation reaction, "acute" changes may occur months after exposure. Acute here is used to indicate the initial reaction to injury: necrosis

and inflammatory change, as distinguished from the later proliferative process of repair. In all tissues reactions following irradiation are slower than most inflammatory responses, and such changes as fibroblastic proliferation may be a part of the initial response to irradiation.

The earliest roentgenographic change seen in our cases was an increase in radiolucency of the chest. This, as in Case XIX, may be followed after an interval of a few weeks by an increased density, part of which is apparent as discrete bands, with displacement of the trachea, heart, and mediastinal shadow toward the affected side (Fig. 7). This early radiation reaction is comparable to that seen in other tissues, such as the skin or mucous membrane and can be expected in some cases to show complete regression and in others to show a residual fibrosis of the lung with or without pleural fibrous adhesions, depending upon the degree of injury and subsequent treatment. The acute reaction may be readily differentiated from infectious lesions by the distinct linear bands associated with the traction of the mediastinum. This usually appears about the same time interval after irradiation that one would expect the height of the cutaneous reaction, although the time is somewhat variable. These distinctive changes also serve to differentiate the process from infiltration of metastatic disease.

Case III developed symptoms of respira-, tory embarrassment four weeks after the second series of roentgen therapy and fourteen weeks after the first. Roentgen examination of the chest revealed rather extensive changes in the lungs limited somewhat to the field irradiated. The small amount of radiation given and the absence of distinctive changes in the film led us to consider infiltration of malignant disease rather than radiation reaction. It must be kept in mind that the later stages of the acute reaction may not be distinctive. Moreover, in view of the known presence of Hodgkin's disease in Case III it was natural to consider this change as due to malignant infiltration and further roentgen therapy was carried out. Study of lung sections of this case two days after the film was taken showed characteristic gross and microscopic changes similar to the other cases of acute radiation reaction.

The late changes representing the resid-

ual fibrosis and hyalinization, often with pleural adhesions and decrease in the size of the thoracic cage, are exemplified by Case xvi. In this phase of radiation reaction one sees fibrous bands as well as vary ing degrees of traction of the mediastinum toward the affected side. Associated with this is a contraction of the thoracic cage on the affected side. This is due in part to decrease in size of the lung and in part to dense pleural adhesions to the contracted lung. In metastatic disease there is no decrease in size of the thoracic cage, and if pleural involvement occurs as a result of tumor metastasis this is practically always associated with pleural effusion. It is of real value that we can demonstrate radiation changes roentgenologically even in the presence of metastasis. While this often cannot be determined with a single roentgenogram, nevertheless, with serial films it is usually possible to differentiate the development and passing of a radiation reaction from the presence of metastatic disease. Roentgenoscopic studies, lateral chest films and Potter-Bucky films are helpful in distinguishing between radiation pneumonitis and metastatic disease. The percentage of metastasis was the same in both irradiated and non-irradiated groups: 62 per cent and 63 per cent respectively.

The amount of radiation necessary to produce histologic reactions varies greatly, although in most instances heavy dosage is required (Table 11). This, together with variations in time and rate at which treatment is given, and the size of the portal, suggests that there are factors other than irradiation alone concerned in the development of these lesions. The variability of time in the development of even the acute lesions is striking. Thus, in the cases showing lesions of the acute type the interval from the first treatment to death ranged from 10 days to 100 weeks and between the last treatment and death the time ranged from one day to twenty-two weeks. In the cases showing combined acute and late types of reaction, the time interval ranged from 11 weeks to 455 weeks from

# MAY, 1940

## TABLE II RADIATION CASES

·				•	•	RADI	ATION (	CASES						•
	Gener	I					Mic	10800	pic A	haly	eis		-	
	Gener	a.			Alve	olar Fil	orosis	<u>.</u>		Arter	ial Ch	anges		•
Total Radiation	Case No.	Age	Sex	Time between Last Treat- ment and Death	Exfoliation of Epithelium	Diffuse	Focal	Hyaline	Intimal Fibrosis	Metastasis	Edenia	Pleural Fibrosis	Hyaline Membrane	
16,000–15,000 r	xx	35	ę	8 weeks			+	+	-+	+	_			Acute and late suggestive
13,000 r	XVI	62	ਰਾ	9 weeks	+	+	++	++	+				++	Acute and late definite
9,000- 8,000 r	XIV XIII	39 70 68	<b>♀</b> ************************************	I week 4 weeks 12 weeks	++	+++	++++	.+ ++ +	+	++	+	+	+	Acute and late definite Acute and late definite Acute and late suggestive
8,000-7,000 r	xxII xIX*	52 55	Р Р	26 weeks 29 weeks	++	+	+	+	+	++	+	+		Acute and late definite Acute and late suggestive
7,000- 6,000 r	I 'x xv	58 55 43	<b>Q</b> Q	16 weeks 3 days 12 weeks	+	+	++	+	+	+	++		+	Acute definite Acute and late definite Acute and late definite
6,000- 5,000 r	XXVI	64	φ	33 weeks			+	+		_+				Late definite
5,000- 4,000 r	n xii xxiii xxvii•	52 54 59 66	Q+ Q+ Q+ Q+	8 weeks 8 weeks 20 weeks 18 weeks	++++++	+	++ + +	+++++	+	++	++		++++	Acute definite Acute and late definite Acute and late definite Late suggestive
4,000- 3,000 r	v vi xi	79 53 50	<b>™</b> 0 % 0-	10 days 2 weeks 8 weeks	+++	++	++	+++		+	++		+	Acute suggestive Acute suggestive Acute and late definite
3,000- 2,000 r	XVII XVII	55 61 41	~ 75 0+	1 day 5 weeks 130 weeks	+++	+ + +	++++	+++++	++	++	++		+	Acute and late definite
2,000- 1,000 r	XXIX XXIX XXIX	47 49 64 46	O+ O+ O+ No	52 weeks 16 weeks 52 weeks 5 weeks	+	+ +	+	+	+	++	+	+++	+++	Late suggestive
600 r	IV	86	Ş	6 days	+	+					++		+	Acute definite
						Radi	um							
10,000 r x-ray and 13,861 mg-hr. radium	xxv	57	}	12 weeks	++	++	+	++	+	+	-	++		Late definite
12,000 r X-ray and 17,320 mg-hr. radium	ΔΠ	45	Ç	12 weeks	+			+		+	+	+	++	Acute suggestive
23,112 mg-hr.	XXVIII	53	₽	1 week	+++		+++	++	+					Late suggestive
					No Ro	entgen l	Radiati	on 						
		43 67 76	<sup>7</sup> 5 ♀ ♀		+ + +	+++++++		+ +	+	+	++++		+	

<sup>\*</sup> This case was first observed clinically. It is not one of the group of 398 cases studied primarily from the histologic angle.

<sup>†</sup> Lead therapy also.

the time of the first treatment to death. The time interval from the last treatment to death varied from three days to twelve weeks. In view of this wide variation, it can be deduced that in the lung as in the skin there is a wide range of time in which radiation reaction may develop. The variation in development of radiation reaction of the lung is comparable to that seen in tissues subjected more directly to radiation as in intracavitary therapy of the cervix. Hence, even though pulmonic changes sometimes appear long after treatment, radiation pneumonitis should be ruled out before assuming that they are due to metastatic disease.

The question naturally arises as to why some cases which have received comparable amounts of radiation fail to show roentgenographic or histologic evidence of radiation reaction. In an effort to learn what the determining factors might be, the cases were considered from the standpoint of age, thickness of chest wall, whether or not amputation of the breast had been performed, and the presence of pneumonia.

• TABLE III
• THE EFFECT OF PULMONARY ALTERATION ON PULMONARY RADIATION REACTION

	Meta	stases	Pneumonia		
			Pres- ent		
Radiation reaction cases Cases without radiation	18	11	16	13	
reaction	136	72	76	131	

The thickness of the chest wall appeared to have no particular significance (Table IV). Thus, of the cases developing radiation reaction, 15 had a thick wall and 14 a thin chest wall. Of the cases with no radiation reaction, 104 had a thick chest wall and 102 a thin chest wall. Amputation of the breast also made comparatively little difference, 18 of those with radiation reaction having both breasts present and 11 having one amputated on the affected

side, whereas among the group showing no pulmonic radiation reaction, 121 had both breasts and 86 had had a breast amputation. Extraneous factors appear to be of little aid in predicting whether a pulmonic radiation reaction will develop in a given case.

 $\begin{tabular}{ll} Table \ IV \\ \end{tabular}$  the effect of thickness of chest wall on pulmonary radiation reaction

	Ches	st Wall	Breast		
	Thin	Thick	Ampu- tated	Not Ampu- tated	
Radiation reaction cases Cases without radiation	Ι4	15	ΙΙ	18	
reaction	102	104	86	121	

Pneumonia was present in 16 (55 per cent) of the 29 cases showing histologic radiation reaction. It was present in 76 (37 per cent) of the cases without radiation reaction whose lungs had been irradiated. Thus there is a slight but possibly not significant difference. We cannot now say anything in regard to the possible hazard of radiation pneumonitis and whether or not it plays any part in the development of pneumonia.

The average ages of the females in the irradiated and non-irradiated groups were identical, 53.6 and 54.2 years. In the males there was a somewhat older average age for the cases showing radiation reaction, 62.7 years as against 51.4 years. We are indebted to Dr. Sidney Farber for a case showing marked reaction roentgenologically and histologically following irradiation of pulmonic metastases of neuroblastoma in a child aged five.

In attempting to differentiate the histologic characteristics of this condition, one must consider changes due to metastatic tumor, atelectasis, complete or partial bronchial obstruction, vascular changes, and to various inflammatory conditions. The features of the acute reaction are three-fold: (1) the striking deposition

of fibrin-like material in the alveoli, often tending to form a hyaline, membrane, which may be continuous with the fibrous tissue of the alveolar walls; (2) the swelling and destruction of alveolar lining cells, the survivors being distorted to oval or elongated, swollen bizarre cells, frequently very large and multinucleated; (3) the marked edema. These changes differ from those seen in any of the usual pneumonic processes by the absence of inflammatory cell reaction commensurate with the intensity of the cell changes and edema.

This hyaline membrane is the most definite of all the changes and we have used this primarily in sorting out irradiated from non-irradiated lungs. This membrane is usually distinguished from hyaline change of fibrin masses seen especially in aspiration pneumonia. It is more closely adherent to the alveolar wall, less fibrillar, and more homogeneous than fibrin. The alveoli lined by hyaline are usually much distended in contrast to adjacent alveoli. This membrane is not peculiar to radiation pneumonitis. In the pneumonic form of bubonic plague, 16 a fibrinous membrane may occur at the periphery of the alveolus, but is accompanied by masses of bacteria and hemorrhage. In influenza the hyaline membrane is associated with interstitial emphysema,20 and frequently acellular or hemorrhagic exudation.<sup>17</sup> In a case dying of an influenza pneumonia, not included in our series, the hyaline membrane was marked and indistinguishable from that seen in the most clear-cut radiation pneumonitis. The early stages of chemical pneumonia (mustard gas, etc.) show at first a hyaline membrane with vascular engorgement, rapidly followed by necrosis and small abscesses.7

In the late reaction the vascular change is a help in diagnosis. The marked hyaline fibrosis and the vascular alteration produce not only great thickening of the alveolar walls and resultant separation of the alveolar capillaries, but distinct diminution of the lumina of the larger vessels as well. The latter show the hyalinization and fibrosis

of their coats so commonly seen in irradiated vessels elsewhere. There is a diffuse fibrosis of the septa, often focally accentuated, and rarely foci of necrosis of collagen. Late reactions vary in intensity, as seen in Case XIX, in which there is only very slight residual fibrosis of alveolar walls and septa. Such changes are frequently seen in old age, and are not pathognomonic of irradiation.

### ILLUSTRATIVE CASES

Case III (H. H. 37-313). This case illustrates acute radiation pneumonitis. White female, aged fifty-five, was admitted to the hospital September 30, 1936, complaining of dry cough of one month's duration. She was of exceptionally slight build, weighing about 85 pounds. The onset of her present illness was six months prior to admission, consisting of abdominal pains and eructations. Three months before admission the patient had noted a swelling in the neck and thereafter began having night sweats and occasional chills. She also noticed that she readily became fatigued, necessitating her going to bed. After two months she developed a dry cough, sore throat, and became dyspneic. There was some pain throughout the chest, especially on deep inspiration. Physical examination was essentially negative except for several cervical nodes 1 to 3 cm. in diameter and some dullness at the right base. The white blood count was 16,150, the red cell count 4,790,000. The urine was normal. Roentgen examination of the gastrointestinal tract was normal. A roentgenogram of the chest revealed increased density at the cardiohepatic angle. A biopsy of a node in the neck was reported as Hodgkin's disease.

Between October 2 and 10 inclusive, the patient received 600 r to the anterior, and 600 r to the posterior chest through a large portal at 50 cm. focal skin cistance, and in addition irradiation to the enlarged cervical nodes. The other factors used were 0.5 mm. copper filter, 200 kv. (peak). On December 14, 1936, the patient was again admitted to the hospital complaining of a constant cough and pain in the lower back. Roentgen examination of the chest showed no changes. In view of the symptoms, the patient received an additional 600 r to the anterior, and 600 r to the posterior chest, using a 20×20 cm. portal.

slightly flattened epithelial cells. The vascularity is diminished, and those vessels present show varying degrees of fibrosis, edema, and hyalinization of their walls. Some vessel walls are five times the usual thickness. There is scattered anthracotic pigment throughout, and scattered clusters of tumor in lymphatics, chiefly perivascular. Bronchial walls are fibrosed.

Case xvi (Pondville 36-A-169). This case shows a severe acute reaction superimposed on a late reaction. The patient, a white male, aged sixty-two, was first admitted December 27, 1935, to the Boston Dispensary, complaining of a growth of the left breast which had gradually increased in size during the past four months.

Local examination revealed a diffuse infiltrating carcinoma involving the left breast extending over the pectoral muscles to the axilla and adjacent chest wall. There were multiple skin nodules involving the left chest wall. In the left axilla there were large metastatic nodes, and also several nodes above the left clavicle

Roentgen examination of the chest showed no evidence of metastases nor of fibrosis.

Between December 27, 1935, and January 6, 1936, the patient received 1,200 r produced at 180 kv. (peak), directed to the left anterior chest, and 1,200 r to the left lateral chest, 300 r daily, using a large portal. Using a 10×10 cm. portal, 900 r was directed to the supraclavicular region. After an interval of two weeks, an additional 1,200 r was given to the left chest and axilla through two portals, and 800 r directed to the supraclavicular region. At irregular intervals, further irradiation was given until June 19, 1936. The total radiation to this date was 7,400 r.

Roentgen examination of the chest revealed a diffuse thickening of the left mid-lung field with pleural adhesions at the base. The changes were thought to be fibrosis as the result of irradiation (Fig. 4). On this date the patient complained of a slight cough. The disease involving the left breast and chest wall showed some regression.

On August 10, 1936, the patient was admitted to the Pondville Hospital and additional radiation was given, a total of 3,600 r, 300 r daily, directed to the anterior, lateral, and posterior left chest.

Roentgenogram of the chest three weeks following completion of this series of treatments showed no change since examination in June. However, a film of the chest taken October 6, 1936, five weeks after last treatment, showed

an increase in the changes in the left lung field and some increased density in the right lung root (Fig. 5). These changes were erroneously thought to be pulmonary metastases, and additional radiation totalling 2,400 r was given during the next nine days to the chest, making a grand total of 13,400 r. Following this the patient left the hospital against advice.

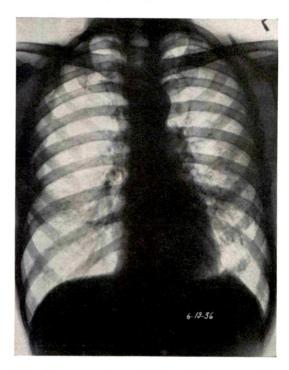


Fig. 4. Roentgenogram of chest of Case xvi, after six months of radiation therapy. Note diffuse thickening in left lung field and adhesions at base.

The final admission was on December 3, 1936, at which time the patient complained of continued weakness, and showed signs of progressive inanition until his death on December 24, 1936, nine weeks after the last treatment.

The significant autopsy findings were: A well-developed but extremely emaciated male, showing marked tanning and atrophy of the skin of the thorax, with numerous small tumor nodules.

Pleural cavities: Posterior and lateral aspects of lungs bound to chest wall by dense pleural adhesions. These are tough, fibrous, and are torn loose only with difficulty.

Lungs: Left lung weighs 275 grams. Right lung weighs 300 grams. The outer surface of the right lung is bluish-gray and somewhat mottled in appearance and there are a few

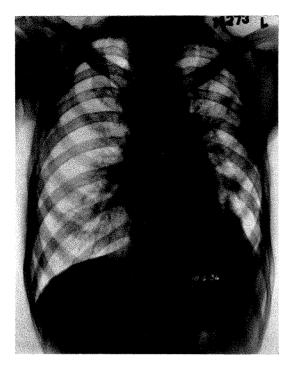


Fig. 5. Roentgenogram of chest of Case xvi, after nine months of radiation therapy. Note increased density of lung fields, especially on left.

tough fibrous tags adherent. The bronchi are diffusely injected. The pulmonary vessels show minimal yellow intimal streakings. On section of the lung, it cuts with increased difficulty. The lower lobe is partially collapsed and is somewhat gray and opaque in appearance. The upper lobe is much more crepitant than the lower lobe and is grayish-red in appearance. The left lung is similar to the right except in section. The lower lobe is firm and on section it is uniform gray with slight yellowish streaks through it. There are adhesions between the upper and lower lobes and the upper lobe itself is crepitant and grayish-pink in appearance.

Microscopic examination: Throughout, fibrosis is extensive, obliterating lung markings in many zones. Edema is definite in almost all regions. Early as well as late organization is present. The walls of the alveoli are markedly thickened and some are represented by eosinophilic hyaline bands.

Many alveoli are diminished in size and some have been entirely obliterated by partially hyalinized fibrous tissue. Many of the smaller persisting alveoli are lined by epithelium sometimes curiously distorted or multinucleated, sometimes cuboidal or elongated. Occasionally foci of lipoid-filled macrophages are seen. There are rare small foci of necrosis with file in-like depositions in the denser connective tissue regions. Throughout, the connective tissue is relatively acellular. Blood vessels large and small show marked subintimal thickening and some endothelial proliferation. The capillary lumen is diminished and the alveolar capillaries are separated widely from one another, giving a very definite reduction in the vascular bed.

The arterioles and venules as well as the larger vessels show a marked degree of fibrosis and hyalinization of their walls, not infrequently with regions of mucoid degeneration and a marked diminution in their lumina (Fig. 6). The bronchi and bronchioles show some hyaline fibrosis of the submucosal and peribronchial tissues. The cartilage is unaltered. There is no change noted in the bronchial epithelium or in the mucosal glands. No evidence of tumor noted.

Case XIX\* (N.E.D.H. 37789). This case is of unusual interest from the clinical standpoint. White female, aged fifty-two, was seen at the Huntington Hospital on May 11, 1937. The chief complaint was a lump in the left breast of five months' duration. The past and familial history was unessential. There was no history of cough and no skeletal pains. The local examination revealed in the upper outer quadrant of the left breast an indefinite, deeply struated mass slightly adherent to the skin. The nipple was retracted. There was a large mass of nodes 8 cm. in diameter in the anterior axilla,

\* This case was first observed clinically. It is not one of the group of 398 cases studied primarily from the histologic angle.

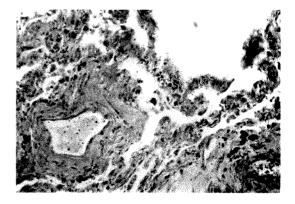


Fig. 6. Photomicrograph of involved portion of lung of Case xvi, showing thickening and hyalinization of vascular walls, atypical alveolar lining cells and thickening of alveolar walls.

and a few 2 to 4 cm. nodes over the left clavicle.

Roel tigen studies of the chest, skull, and pelvis were normal. Between May 12 and June 4, the patient received 2,000 r to the left anterior chest and axilla, using a 15×15 cm. portal; 1,600 r to the left supraclavicular area, using a 10×10 cm. portal. The treatments were given in exposures of 400 r daily, using 1,000 kv. (peak) and 70 cm. focal skin distance. At the completion of the treatments no reaction had developed, and there were no new symptoms.

The patient was seen again on June 15. A definite erythema had developed over the left clavicle, and a faint erythema over the left breast and chest. A roentgenogram of the chest showed both lung fields clear with increased radiolucency of the left chest. An additional dose of 2,500 r was given, directed to the left breast and axilla. After an interval of one week, the radiation reaction had increased in intensity, and the masses in the breast, axilla, and supraclavicular region had shown regression. Since the general condition of the patient was satisfactory, 2,400 r additional was given. The roentgen dosage was measured in air with a Victoreen r-meter.

Examination on July 8, the date of the last treatment, showed a desquamation of the skin over the left chest and axilla. There was a slight cough.

Summarizing the irradiation from May 12 to July 8, the patient received a total of 7,900 r directed to the left chest and axilla. In addition, 2,000 r was given to the left supraclavicular area, all in exposures of 400 r each.

The patient was again seen on July 27, at which time she reported a slight cough of about two weeks' duration. Roentgenogram of the chest showed in the peripheral zone of the left upper lung a few ill-defined foci of increased density which were interpreted as changes due to the irradiation.

During the following month, patient continued with a dry cough which gradually improved and the general condition remained unchanged. She was up and about and able to play golf without developing dyspnea. Roentgenogram of the chest on August 31 revealed a diffuse dullness involving the upper half of the left chest. The heart, mediastinum, and trachea were displaced toward this side. Roentgen examination at this time revealed a metastatic focus in the skull and also in the pelvis.

On September 24, the pain in her left hip became so intense she was unable to walk. Roentgen studies of the pelvis revealed a large osteolytic metastasis in the left sacroiliac joint. The changes in the chest demonstrated

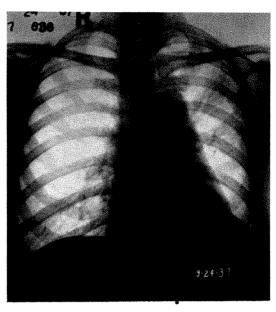


Fig. 7. Roentgenogram of chest of Case XIX, three months after irradiation was started and one month after last treatment. Note radiation changes in upper left chest, with displacement of heart, mediastinum and trachea to left.

twenty-four days previously had not changed appreciably; however, there was suggestive evidence of diminished density (Fig. 7). Palliative irradiation was given over the pelvis for the relief of pain. The patient was never able to get out of bed after this. The disease in the breast increased in extent. Multiple skin metastases developed over the left chest, extending over the left arm to the elbow. Several nodules developed over the skull and a pathological fracture of a rib occurred. The patient gradually failed, and died on January 9, 1938.

The significant findings at autopsy were as follows: Development and nutrition were good. Weight 130 pounds.

Pleural cavities: Right has a few fibrous adhesions binding lower portion of lung to diaphragm. Rest of surfaces on this side smooth, glistening, slightly injected. Left contains approximately 10 cc. of turbid, straw-colored fluid. Surfaces injected, smooth, glistening except laterally over left lower lobe. Here a thick layer of fibrin binds lung to chest wall.

Lungs: Right 320 grams, left 420 grams. Upper lobes of both lungs slightly subcrepitant. Cut surface gray, mottled with black. Small amount of frothy fluid exudes from cut surfaces. Bronchi patent throughout and contain small amount of thin, frothy fluid. Both lower lobes deep red, definitely subcrepitant, exude much bloody, frothy fluid on slight pressure and show foci of consolidation about smaller bronchi.

Bronchi in these lobes filled with thick, turbid material. Bronchial mucosa is red and finely granular. In the left lower lobe is an ill-defined, soft, gray focus 1.5 cm. in diameter.

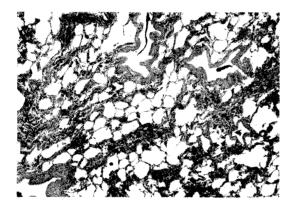


Fig. 8. Photomicrograph of involved portion of lung of Case xix. Note slight fibrosis and hyalinization. ×48.

Microscopic examination: Left upper lobe shows slightly and uniformly thickened and fibrosed pleura. Alveoli empty. The alveolar lining cells are inconspicuous, the alveolar walls slightly fibrotic, the hyalinized connective tissue somewhat dense. This results in an apparent slight lessening of the vascularity of the lung parenchyma. Bronchi contain finely granular material and cellular debris. Epithelial surfaces negative. Bronchial walls slightly fibrosed. Endothelium of blood vessels inconspicuous. Media somewhat edematous in both arteries and veins. A few veins contain mural thrombi. Smaller arterioles present hyaline thickening of their walls. Most of larger vessels show definite fibrous thickening of their walls, usually with some degree of hyalinization (Fig. 8). Left lower lobe shows a similar condition except that the alveoli are filled with finely granular material, polymorphonuclear leukocytes, and a scattering of lymphocytes and mononuclear phagocytes. Some alveoli partly

lined by large, pale-staining, oval cells and a few alveoli contain fibrin and cellular debris. Among the exudative cells are scattered vacuolated macrophages. Some of the more heavily affected alveoli contain coarse strands of fibrinoid substance which extend into the connective tissue of the alveolar walls. In scattered foci alveolar lining cells have disappeared or have rarely been replaced by large irregular elongated cells. Bronchi contain similar exudate and show some necrosis of lining epithelium. Right upper lobe shows irregular septal fibrosis and most of alveoli contain a small amount of finely granular material, though a few bordering on bronchi are filled with polymorphonuclear leukocytes, a few lymphocytes and some cellular debris. Bronchi contain similar material and show slight fibrosis of walls. Foci of parenchymal fibrosis with inclusions of large, oval, deeply stained cells are also present. Blood vessels are negative. Right lower lobe somewhat similar to left lower lobe except that inflammatory reaction is more marked and more alveoli are lined by epithelial cells and there is less fibrosis of alveolar walls. No evidence of tumor is found.

Three of the 4 preceding cases we have selected to illustrate the three types of reaction encountered: the acute, the late. and the late with superimposed acute changes. Case XIX illustrates the slight. nonspecific changes that may be present after very heavy irradiation and is our only case which has definitely shown a transient reaction as proved at autopsy. From the postmortem studies it would appear either that transient changes resulting from irradiation are not distinguished from other inflammatory conditions or that our material did not include such cases. Considering the wide range of material used in the study, the former seems most likely.

#### DISCUSSION

This study of radiation pneumonitis from clinical, roentgenologic, and postmortem aspects in an unselected series of 234 patients has served to clarify observations made by roentgenologists as well as to present the sequence of histologic changes underlying the reaction.

The roentgenologic findings in radiation pneumonitis are best interpreted after correlating the clinical course following irradiation with frequent roentgenograms of the chest. It is desirable to have roentgenograms of the chest before irradiation is started, and frequent examinations during the course of the reaction. Under these conditions pulmonary changes due to irradiation can usually be readily differentiated from infections and metastatic processes of the lungs. The practical importance of this type of change is illustrated by Case III of McIntosh<sup>12</sup> and our Case III where the additional radiation given under the assumption that the lung changes were due to metastases may well have been a contributing factor in the death.

The frequency of pulmonic change increases as does the amount of radiation delivered to the chest, but not with any regularity. The majority of the cases showing radiation reaction present symptoms of an unproductive hacking cough during the height of the local skin reactions.

The histologic aspects of the study have been further checked by examination of a control series of 1,060 unselected autopsies from Pondville Hospital from 1929 to 1937 (excluding those used in our initial series of 398 cases taken in part from Pondville Hospital). This control group was handled in the same way as the study group. The histologic diagnosis of radiation pneumonitis was confirmed in 4 cases by the history. There were 3 cases with histologic changes typical of radiation pneumonitis which had not been irradiated. In 5 cases in which there were some suggestive features there had been no irradiation. This percentage of error (0.7 per cent) is as low as can be achieved in differentiating the cause of any histologic reaction not accompanied by the presence of a visible agent. An analysis of our errors shows that these have been due in most cases to acceptance of marked change of one type or another as indicative of radiation pneumonitis. This is particularly apt to be misleading when there is

much fibrinous exudate, as in some of the organizing pneumonias.

The sequence of tissue changes following roentgen irradiation of the lungs varies with the amount and kind of radiation. It is probable that the earliest effect is one of mild injury to the alveolar lining cells and the capillary endothelium. Edema, swelling, necrosis, and proliferation of endothelium and alveolar epithelium follow. With injury to connective tissue, fibroblastic proliferation, chiefly in the alveolar walls, occurs. We have not been able to identify peribronchial, septal or pleural fibrosis specifically with radiation pneumonitis.

Our experience shows that appreciable injury and repair of fibrous tissue occur only after very intensive irradiation, the connective tissue apparently being more resistant to roentgen rays than the other tissue elements. The transient radiation pneumonitis long recognized by roentgenologists, and illustrated by our Case XIX, supports this view.

These histologic features of the early reaction, including early fibroblastic proliferation, we have not found distinctive in our cases. With our present knowledge it is not possible to distinguish early acute radiation pneumonitis from other conditions, although very prominent edema and large epithelial and endothelial cells in the absence of much exudate are suggestive of radiation pneumonitis.

When the primary injury is sufficiently severe to affect endothelium, fibrous tissue, and epithelium, the well developed repair process presents a picture which may resemble that following a number of different injurious agents. The vascular change is particularly difficult to evaluate. Fibrous thickening and hyaline swelling of veins and arteries such as are associated with radiation pneumonitis are seen occasionally in youth and more commonly with advancing age, frequently unaccompanied by other disease processes. However, these changes may be restricted to that portion of the lung which presents other evidence

of radiation pneumonitis and which was known to have been included in a field of irradiation.

The only histologic picture which we can with certainty recognize as radiation pneumonitis is that which shows in some degree both these early and late stages in the same lung.

The hyaline membrane which we have emphasized in our classification complicates the subject somewhat inasmuch as we are not at present prepared to describe its manner of formation. It probably represents an acute or subacute response. We feel that this hyaline membrane is the surest guide in diagnosis of radiation pneumonitis. We have rarely been misled by this membrane except when it was slight or atypical and accompanied by organizing pneumonia. Observation of this with the other changes enumerated makes it possible to recognize with accuracy the cases which have received irradiation to the chest. In a few cases we have been led to suspect post-irradiation changes without the presence of the hyaline membrane, only to find that irradiation had not been given. We have found that the other changes we have enumerated as part of radiation pneumonitis are less distinctive and not as easily differentiated from infectious processes.

It is obvious that in going over such a large series of slides accurate grading of relative changes of different types, as fibrosis, edema, endothelial swelling, blood vessel changes, would be an extremely laborious and impractical task. But such a study carried out by a single observer of both gross and microscopic specimens would be of definite value. And it is only by this method of study that we may hope to learn something of the history of cell changes initiated by irradiation.

The fact that a great many heavily irradiated patients show no recognizable reaction makes us feel certain that we still have a good deal to learn of the way in which the lung reacts to irradiation, and the possible hazard of such a reaction. Its

relation to pneumonic infections is a particularly important and intriguing question which we are at present unable to answer. We would make this report a plea for more discriminating study of this subject by both radiologists and pathologists. We hope that experiments now being carried on will further clarify the subject.

### SUMMARY AND CONCLUSIONS

1. By histologic study of the lungs of an unselected series of 398 autopsied cases of malignant disease primary between diaphragm and neck it has been possible to collect 29 cases (7 per cent of the entire group, 12 per cent of 234 irradiated cases) which showed changes referable to irradiation of the lung. An erroneous diagnosis of radiation reaction was made in 3 cases which it was found later had not received irradiation to the chest. In a consecutive series of 1,060 autopsies (1929-1937) from Pondville Hospital, exclusive of the cases in the first group, there was a 99.3 per cent accuracy in diagnosis of radiation pneumonitis based solely on histologic changes.

2. From the standpoint of its reaction to irradiation the lung should be considered as a highly vascularized mucous membrane of relatively low density.

3. A certain combination of tissue changes presents a histologic picture which is practically pathognomonic for radiation pneumonitis, although the units of cellular and humoral change which make up this picture may be found in other conditions.

4. Tissue reactions most closely simulating radiation pneumonitis are found in: chronic nonspecific interstitial pneumonitis; influenzal pneumonia; chemical pneumonitis; all of which are extremely rare.

5. It is probable that certain stages of radiation response in the lung have not been recognized histologically, and may be of such a nature that differentiation from other disease processes is impossible.

6. The changes may be divided either on pathologic or roentgenographic grounds into three stages: acute, late, and late with superimposed acute reaction.

- 7. Chest roentgenograms were available in 115 of the 234 cases, but in only 62 cases were they suitable for this study. In only 5 (8 per cent) were there roentgenographic changes definitely due to irradiation. It seems fair to assume that this is not a true index of the frequency of pulmonic reaction. Were radiation changes watched for from the time of beginning therapy, study both antemortem and at autopsy would give a higher percentage of cases showing reaction.
- 8. Radiation reaction is sometimes slight and may not permanently affect the lung.
- 9. The amount of radiation alone does not determine the development of a radiation reaction, although the proportion of lungs showing changes increases with the amount of radiation.
- 10. Variables such as the thickness of the chest wall, amputation of the breast, the existence of pulmonary metastases, the existence of pneumonia, were considered and found to have no significant relation to the development of radiation changes.
- 11. Age is not a factor. In females no significant correlation with age occurs. In males there was a somewhat higher average age for the cases showing radiation reaction, sixty-five years as against fifty-one years, probably a chance variation.
- 12. Criteria are given for the differential diagnosis of radiation reaction by roent-genographic and pathologic means.

### REFERENCES

- Bergonié, J., and Tessier. Rapport sur l'action des rayons X sur la tuberculose. Arch. d'électric. méd., 1898, 6, 334–360.
- Desjardins, A. U. Action of roentgen rays and radium on the heart and lungs. Am. J. ROENTGENOL. & RAD. THERAPY, 1932, 28, 701-720.
- 3. Downs, E. E. Lung changes subsequent to irradiation in cancer of the breast. Am. J. Roentgenol. & Rad. Therapy, 1936, 36, 61-64.
- ENGELSTAD, R. B. Die Strahlenreaktion in dem Lungen beim Menschen. Acta radiol., 1937, 18, 32-43.
- Evans, W. A., and Leucutia, T. Intrathoracic changes induced by heavy radiation. Am. J. ROENTGENOL. & RAD. THERAPY, 1925, 13, 203-220.

- FIKE, R. H. The occurrence of roentgen pleuropneumonitis in treatment of breast cancer. Am. J. RÖENTGENOL. & RAD. THERAPY, 1932, 27, 509-512.
- GILCHRIST, H. L., and MATZ, P. B. The residual effects of warfare gases; use of chlorine gas, with report of cases. M. Bull. Vet. Admin., 1933, 9, 229-270.
- GROOVER, T. A., CHRISTIE, A. C., and MERRITT, E. A. Intrathoracic changes following roentgen treatment of breast carcinoma. Am. J. ROENTGENOL. & RAD. THERAPY, 1923, 10, 471-476. Observations on use of copper filter in roentgen treatment of deep-seated malignancies. South. M. J., 1922, 15, 440-444.
- HINES, L. E. Fibrosis of the lung following roentgen-ray treatments for tumor. J. Am. M. Ass., 1922, 79, 720-722.
- 10. HSIEH, C. K., and KIMM, H. T. Changes in lungs and pleura following irradiation of extrathoracic tumors. Am. J. ROENTGENOL. & RAD. THERAPY, 1937, 37, 802–810.
- II. KÜPFERLE, L. Experimentelle Untersuchungen über die Röntgenbehandlung der Lungentuberkulose. Strahlentherapie, 1912, 2, 590– 597.
- McIntosh, H. C. Changes in lungs and pleura following roentgen treatment of cancer of the breast by prolonged fractional method. Radiology, 1934, 23, 558-566.
- McIntosh, H. C., and Spitz, S. A study of radiation pneumonitis. Am. J. Roentgenol. & RAD. Therapy, 1939, 41, 605-615.
- RAJEWSKY, B. Researches in the problem of radium poisoning and the tolerance dose of radium. *Radiology*, 1939, 32, 57-62.
- 15. Strong, R. P., Crowell, B. C., and Teague, O. Studies on pneumonic plague and plague immunization. vII. Pathology. *Philippine J. Sc.*, 1912, 7, 203–221.
- WARREN, S. L., and WHIPPLE, G. H. Roentgenray intoxication. I. Unit dose over thorax negative—over abdomen lethal. Epithelium of small intestine sensitive to x-rays. J. Exper. Med., 1922, 35, 187–202.
- 17. WINTERNITZ, M. C., WASON, I. M., and Mc-NAMARA, F. P. The Pathology of Influenza. Yale University Press, New Haven, 1930.
- WINTZ, H. Injuries from roentgen rays in deep therapy. Am. J. ROENTGENOL. & RAD. THER-APY, 1923, 10, 140-147.
- 19. WOHLAUER, F. Der Einfluss der Röntgenstrahlen auf das Lungengewebe. *Deutsche med. Wchnschr.*, 1909, 35, 1704–1706.
- 20. Wolbach, S. B. Comments on the pathology and bacteriology of fatal influenza cases, as observed at Camp Devens, Massachusetts. *Bull. Johns Hopkins Hosp.*, 1919, 30, 104–109.

### PRIMARY LYMPHOSARCOMA OF THE HARD PALATE

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PRIMARY lymphosarcoma of the hard palate is extremely rare. In a review of the literature since 1893, when Kundrat<sup>17</sup> established lymphosarcoma as a disease entity, only one case was found which was limited to the hard palate. Although numerous instances of lymphosarcoma of the hard palate have been published, 4,11,17,20,22 all of these were secondarily involved by contiguity from lesions of neighboring structures. Chaton's case<sup>6</sup> is the only exception. During the past ten years, 108 patients with lymphosarcoma have been registered at the Mount Sinai Hospital. The case reported below was the only one with primary involvement of the hard palate.

#### CASE REPORT

P. F. (O.P.D. No. 38-69), white, male, aged fifty-four, was admitted to the Out Patient

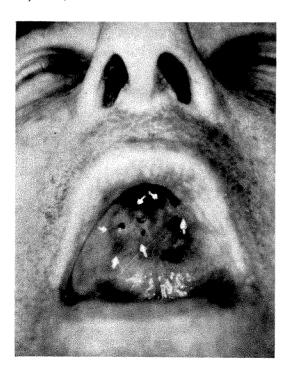


Fig. 1. Photograph taken on March 22, 1938.

\* Assistant Radiologist, The Western Pennsylvania Hospital, Pittsburgh, Pa.

Department of the Mount Sinai Hospital on January 4, 1938.

Present Illness. The patient noted a tender, raised "sore" on the hard palate three months before admission which was slowly progressing in size. He had worn a full upper denture for five years, but because of breakage, none was worn for eight months prior to admission. The patient reported infrequent headaches, pain over the malar bones, nasal obstruction and constant post-nasal drip. Generally, his appetite was good, he maintained his weight and slept well. There was no familial history of cancer.

Physical Examination. The patient was well-developed and nourished. He was cooperative. There were two granulomatous circumscribed nodules situated in the anterior half of the hard palate. Both were superficially ulcerated. The larger nodule measured 1 cm. in diameter and was to the right of the midline. The smaller nodule measured 0.5 cm. in diameter. It was situated more anteriorly and to the left of the midline (Fig. 1).

In addition, the patient had bilateral sinus disease and multiple nasal polypi; these polypi were also present in the nasopharynx. There was no regional adenopathy. The chest and abdomen showed no gross evidence of disease.

Laboratory Findings. Hemoglobin 83 per cent (Sahli); red blood cells 4,250,000; white blood cells 8,950, with a differential count of 62 per cent segmented and 4 per cent non-segmented polymorphonuclear cells, 29 per cent lymphocytes, 4 per cent monocytes and 1 per cent eosinophiles. Blood Wassermann reaction was negative.

Roentgen examination of the hard palate with an occlusal film showed no abnormalities. Roentgen examination of the paranasal sinuses revealed marked clouding of all of the sinuses. Roentgenograms of the chest showed no abnormality in the heart, lungs or mediastinum.

The report of the first biopsy of the lesion on the hard palate was as follows: "(61641) Fragment of mucous membrane showing chronic inflammation and epithelial hyperplasia" (Drs. P. Klemperer and S. Otani).

Course. A provisional diagnosis of nonspecific granuloma was made. Therapy consisted of mouth washes with sodium perborate, liquor alkalinis antisepticus and topical applications of 10 per cent silver nitrate. At first, there seemed to be slight improvement. However, the subsequent course over a period of six weeks showed gradual progression in size.

Biopsy was repeated March 18, 1938: "(62182) Specimen consists of a small fragment of mucous membrane from the mouth. The surface is covered by a slightly thickened squamous cell epithelium having a hornifying layer on its free surface. The submucosa is diffusely infiltrated by cells which are mostly round and more or less uniform. The predominant cell type corresponds to the medium-sized lymphocyte. There are, however, occasional atypical cells and an occasional mitotic figure. Diagnocis: Lymphosarcoma" (Drs. P. Klemperer and S. Otani) (Fig. 2).

Radiotherapy was begun on March 22, 1938. There were 1,800 r (measured in air) delivered to the lesion with the following factors: 200 kv. (peak), 25 ma., 40 cm. distance, Thoraeus filter (0.4 mm. Sn, 0.5 mm. Cu, 4.0 mm. Al), with a half-value layer of 1.8 mm. Cu. These factors produced 22 r per minute. There were 200 r delivered daily through an intraoral cone with a field size of 4.5 by 3 cm.

A week following the last treatment, bilateral nasal polypectomy was performed. Sections of removed tissue were reported "mucous polypi" (62407). Three additional daily treat-

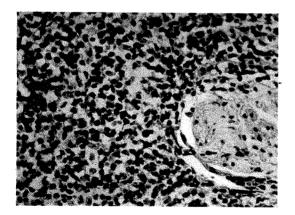


Fig. 2. Photomicrograph of submucosa in the deepest portion of the biopsy section. At the extreme right there is noted a cut nerve around which the diffusely infiltrating lymphosarcoma cells can be seen

ments of 200 r each were then administered. Total dose to the lesion on the palate was 2,400 r (measured in air). The tumor had practically disappeared twenty days following onset of therapy. At this point, the 600 r additional, mentioned above, were delivered. The reaction was most marked on the sixteenth day and was

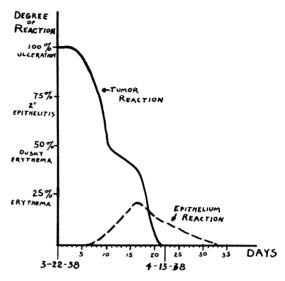


Fig. 3. Response to radiotherapy. The continuous line indicates the tumor size. The interrupted line represents the degree of tissue reaction.

represented by a mild erythema. The reaction faded gradually and disappeared on the thirty-fourth day, or eleven days following the last treatment. Figure 3 illustrates the reponse to irradiation.

In December, 1938, the patient again reported nasal obstruction and post-nasal drip. Examination revealed recurrent nasal polypi. A partial shrinkage of the polypi with marked subjective improvement resulted from radiotherapy directed over the nose and maxillae. The following factors were used: 140 kv. (peak), 20 ma., 0.25 mm. Cu filter, 30 cm. distance with a half-value layer of 0.48 mm. Cu. A total of 800 r per field at 91 r per minute was delivered through portals 5.0 cm. in diameter.

On May 29, 1939, the patient presented a normal mucous membrane (Fig. 4) over the hard palate with pinhead-sized depressions marking the sites of the original ulcerations. There was no significant peripheral adenopathy. Examination of the chest and abdomen showed no gross evidence of disease. Small nasal polypi were present in the left nasal

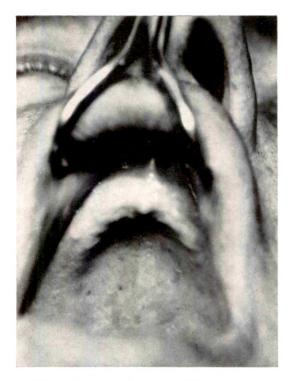


Fig. 4. Photograph taken on May 29, 1939. cavity. The patient's general condition was good.

### DISCUSSION

Differential Diagnosis. Many conditions must be considered in a differential diagnosis of a lesion of the hard palate. Of primary consideration are the inflammatory diseases and the neoplasms. The latter may be epidermal, connective tissue, osseous or dental in origin. Of less frequency, metabolic diseases such as osteitis fibrosa cystica, and osteitis deformans of the leontiasis ossea type may occur. Occasionally, developmental malformations such as a nasopalatine cyst<sup>18</sup> are encountered. Misplaced tissue rests such as aberrant thyroid and dermoid cysts<sup>5</sup> may also occur.

In making the correct diagnosis of a lesion of the hard palate, a careful history and physical examination must be supplemented by hematological, serological, bacteriological and roentgen studies, including occlusal films of the palate. Finally, biopsy will usually be necessary to arrive at the exact type of disease present. This may have to be repeated several times if rep-

resentative tissue is not obtained at first. This is especially true of neoplasms.

Treatment. Surgical excision, electrocoagulation, roentgen and radium therapy have all been used singly or in combination in the treatment of new growths of the palate. Radiation therapy is usually the method of choice in lymphosarcoma. The maintenance of proper oral hygiene is a requisite in the radiation treatment of any mouth lesion. This includes extraction of diseased teeth. There should be limitation of therapy to the lesion either by intraoral cones or by the use of protective devices.<sup>1</sup>

In this case, only roentgen therapy was used. In the case of hard palate lymphosarcoma reported by Chaton, radium element needle implantation was used. He reported complete resolution of existing regional lymphadenopathy without direct treatment of the nodes and marked involution of the local neoplasm. The lymphadenopathy may have been inflammatory. Examination of his patient five months later showed no evidence of malignant disease.

Prognosis. In general, the prognosis of neoplasms of the hard palate is surprisingly good. Bloodgood<sup>3</sup> states, "Lesions of the hard palate are practically identical with those of the gums but are less frequent. Even in cases of long standing and of considerable extent, they rarely metastasize to the lymph glands."

In the case that is being reported, the tumor was slow-growing. For six months prior to treatment, it remained localized to a relatively small area on the hard palate with no extension to regional lymph nodes. The neoplasm was radiosensitive. It disappeared two weeks after the onset of treatment. The patient has been examined routinely every two months since the end of treatment and there has been no recurrence to date, eighteen months after admission.

### COMMENT

In analyzing the rarity of primary lymphosarcoma of the hard palate, the

following explanation is suggested. By definition, lymphosarcoma is a malignant neoplasm arising from lymphoid tissue. Whereas the structures of the oral and pharvngeal cavities such as the posterior nasopharyngeal wall, the fauces, the adenoids, the tonsils, and the soft palate are relatively rich in lymphoid tissue, the hard palate is singularly free of this tissue. Quoting Gray's Anatomy:14 "The palate is covered by a dense structure formed by the periosteum and the mucous membrane of the mouth, which are intimately adherent . . . On either side and in front of the raphe, the mucous membrane is thick, pale in color and corrugated; behind it is thin, smooth and of deeper color; it is covered with stratified squamous epithelium and furnished with numerous palatal glands, which lie between the mucous membrane and the surface of the bone." Schumacher,21 in a detailed histological description of the hard palate, also makes no mention of the presence of lymphoid tissue. Therefore, the paucity of lymphoid tissue in the hard palate explains the rarity of its occurrence at this site.

### SUMMARY

- 1. Primary lymphosarcoma of the hard palate is extremely rare and this is probably due to the fact that, normally, the overlying soft parts are relatively free of lymphoid tissue.
- 2. A case of primary lymphosarcoma of the hard palate is reported which responded favorably to the use of roentgen therapy.

#### REFERENCES

- 1. Ackerman, A. J. Protective shields in radiation therapy of intra-oral cancer. Am. J. Roent-genol. & Rad. Therapy, 1937, 38, 746-754.
- 2. BLAIR, V. P., IVY, R. H. and BROWN, J. B. Essentials of Oral Surgery. Second edition. C. V. Mosby Co., St. Louis, 1936.
- 3. Bloodgood, J. C. In: Practice of Surgery. Lewis, Dean, Editor. W. F. Prior Co., Hagerstown, Md., 1930, IV, Chap. 4, 113.
- 4. BOYD. WILLIAM. Textbook of Pathology. Lea & Febiger, Philadelphia, 1932, pp. 730-736.

- Burchard, H. H., and Inglis, O. E. Textbook of Dental Pathology and Therapeutics. Lea & Febiger, Philadelphia, 1915, p. 70.
- 6. Chaton, M. Lympho-sarcome palatin avec grosse réaction ganglionnaire; disparition complète de la tumeur et de l'adénopathie par le seule radiumthérapie de la lésion principale. Bull. de l'assoc. franç. p. l'étude du cancer, 1923, 12, 448-454.
- 7. CHRISTIANSEN, G. W. Lymphosarcoma of jaws and palate. J. Am. Dent. Ass., 1938, 25, 728-
- 8. CRAVER, L. F. Five year survivals in lymphatic tumors. Surg., Gynec. & Obst., 1935, 60, 485.
- 9. Ewing, J. Neoplastic Diseases. W. B. Saunders Co., Philadelphia, 1928, p. 412.
- 10. Fig., F. A. Malignancies of upper respiratory tract and adjacent structures. Surg., Gynec. & Obst., 1936, 62, 498-502.
- & Obst., 1936, 62, 498-502.

  11. Geschickter, C. F. Tumors of the jaws. Am.

  7. Cancer, 1935, 24, 90-126.
- J. Cancer, 1935, 24, 90-126.
  12. Geschickter, C. F., and Copeland, M. M. Tumors of Bone. American Journal of Cancer, New York, 1936.
- GINSBERG, S. Lymphosarcoma and Hodgkin's disease; clinical characteristics. Ann. Int. Med., 1936, 10, 337-372.
- 14. Gray, Henry. Lewis, Warren, Editor. Anatomy of the Human Body. Lea & Febiger, Philadelphia, 1930, p. 1106.
- 15. HARMER, W. D. Treatment of malignant disease in the upper jaw. Lancet, 1935, 1, 129-133.
- 16. Henke, F., and Lubarsch, O., Editors. Handbuch der speziellen pathologischen Anatomie und Histologie. J. Springer, Berlin, 1927.
- 17. Kundrat, H. Ueber Lympho-sarcomatosis. Wien. klin. Wchnschr., 1893, 6, 211-213; 234-239.
- 18. MEYER, A. W. Quoted by Blair, et al., ref. 2.
- 19. New, G. B., and Савот, C. M. Curability of malignant tumors of the upper jaw and antrum. Surg., Gynec. & Obst., 1935, 60, 971-
- Öhngren, L. G. Malignant tumours of maxilloethmoidal region; clinical study with special reference to treatment with electrosurgery and irradiation. *Acta oto-laryng.*, 1933, Suppl. 19, 1-476.
- 21. Schumacher, S. In: Handbuch der Mikroskopischen Anatomie der Menschen. von Möllendorff, Wilhelm, Editor. Vol. 5, Part 1, 23, J. Springer, Berlin, 1927.
- 22. Shebesta, E. M. Gangrene of the face produced by lymphosarcoma. *Radiology*, 1937, 29, 33-36.
- 23. Takezawa, N. Melanosarkom des harten Gaumens. Oto-rhino-laryng., 1938, 11, 243.

### CARCINOMA OF THE ANUS\*

By ORVILLE N. MELAND, M.D. LOS ANGELES, CALIFORNIA

THOUGH carcinoma of the large bowel has been looked upon as a surgical problem, those malignant lesions found in the region of the anus may be looked upon as an exception. The reasons for such an opinion are based upon anatomical and histological grounds. Therefore, I wish to discuss the problem from the standpoint of the radiotherapist, emphasizing not only

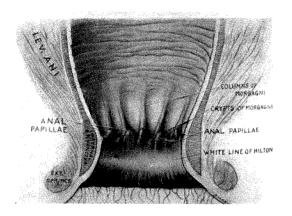


Fig. 1. (From Gant.)

permanency of recovery but also the possibility of retention of physiologic function of the anal sphincter.

### ANATOMICAL CONSIDERATIONS

That part of the terminal bowel which presents itself externally is known as the fixed rectum or anus. Externally it is covered with a loose, coarse, dark-brown pigmented skin, which blends gradually with the skin of the buttocks. Where the junction of the anal skin and the lining mucous membrane takes place (Fig. 1) there is a region known as Hilton's white line; here the skin is soft, smooth, and white instead of pigmented, and covers the region lying between the external and internal anal sphincters. Within the internal sphincter the skin has been replaced by

mucous membrane which is redundant and thrown into longitudinal folds, called the columns of Morgagni, the terminal portions of which make up the anal papillae. Here it is that trauma is greatest and infection, inflammation and fissures occur as a result of chronic irritations of various sorts. The surface cells are of the stratified squamous variety, while farther up they are first transitional and then columnar, and the mucous membrane, instead of being in longitudinal folds, arranges itself in transverse folds. Mucus-secreting glands are numerous in the area covered with columnar epithelium, but not very prevalent in the regions where transitional and squamous cells are found. By reason of these histologic facts, malignant tumors found in this section are practically always epitheliomas, though one may see an occasional adenocarcinoma arising above the columns of Morgagni, while the more rare melano-epithelioma may appear on the skin at Hilton's white line.

A matter of great importance is the lymphatic drainage of these structures. In Figure 2 it can be seen that the collecting vessels from the squamous cell covered mucous membrane run toward the anal skin, anastomosing with the subcutaneous lymph vessels around the buttocks and perineum, emptying into the inguinal nodes. Where columnar epithelium is found, the lymph vessels course upward parallel to the hemorrhoidal veins and arteries emptying into the para-aortic nodes, but at that portion where the bowel wall is covered with transitional cells, a "neutral zone" exists, from which lymph may flow in either direction. When an epithelioma attacks the lower bowel the usual direction for metastasis to pass is into the inguinal nodes; however, if the growth is extensive it may, by direct extension, push into the neutral

<sup>\*</sup> From the Los Angeles Tumor Institute. Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.

zone (Fig. 2) and thus its cells gain entrance into the para-aortic nodes. Likewise, an adenocarcinoma of the rectum proper may grow down into this same neutral zone, giving rise to metastases that are filtered out in the inguinal nodes. These are important when prognosis is under discussion.

### CLINICAL CONSIDERATIONS

In the past fifteen years we have had occasion to examine and treat 260 patients with carcinoma of the terminal colon; of these, 17 had involvement of the anus, giving an incidence of 6 per cent. In these 17 cases we have adequate records for 13 patients; the remainder were terminal cases, so advanced that no treatment, except sedatives, were given; they died very soon after being seen. Though adenocarcinomas may occur here, in these 13 patients, 11 had squamous cell epitheliomas, I had a melano-epithelioma and I was not biopsied. When grading was done, the majority fell into Grades 3 and 4. The sexes were about equally represented, and only one patient was less than fifty years old—the average age was sixty-four years (Table 1).

The complaint most prevalent was rectal bleeding. This symptom was present for from four to twelve months before medical aid was sought; usually the patient had treated himself for hemorrhoids

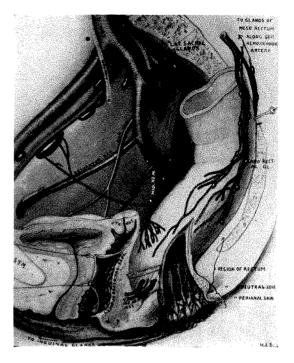


Fig. 2. (From Gant.)

by the insertion of suppositories and by the application of ointments. One patient had pruritus ani for two years before he developed a non-healing ulcer; another had a rectal prolapse for thirteen years before he developed a growth, while a third had rectal distress for forty years, and multiple fistulae for ten years before a tumor was discovered. The common site for the

TABLE I

Case and Year	Name	Sex	Age	Symptoms	Description	Pathology	Treatment	Living	Remarks
1 1922	W	F	7-7-	Bleeding 4 mo.	Ulcer 1 cm. anal margin	Squamous cell epithelioma, not graded	High voltage roentgen therapy anus, 300 r; ra- dium—contact, 1 mm. brass filter, 850 mg-hr.	Yes 7 yr.	Not followed any longer
11 1931	R	F4	70	Bleeding 8 mo.	Firm tumor com- pletely surround- ing anus. Node left groin. Edema left leg	No section taken	Not treated	No	Died in 6 mo.
111 1932	С	М	59	Rectal discomfort 1 yr.	Black, shiny tu- mor at anal mar- gin 2×3 cm. Small implants in sur- rounding skin	Melano- epithelioma	Refused treatment	No	Died in 6 mo.

Table I—Continued

								•	•
Case and Year	Name	Sex	Age	Symptoms	Description	Pathology	Treatment	Living	Remarks
IV 1932	Н	F	65	Bleeding 8 mo.	Tumor 2 ×3 cm. inside sphincter	Squamous cell epithelioma, Grade 3	High voltage roentgen therapy anus, 1600 r; ra- dium—contact, I mm. gold filter, 1600 mg-hr.	Yes 7 yr.	Complains of tight sphincter
v 1934	R	M	65	Rectal prolapse 13 yr.—came on after a hem- orrhoidectomy	Tumor 0.5 cm. anal mucous mem- brane	Squamous cell epithelioma, not graded	Radium-platinum needles interstitially around tumor, 1152 mg-hr.	Yes 5 yr.	Prolapse disappeared as a result of the radiation fibrosis
vi 1935	F	M	70	Itching around the anus with bleeding	Ulcer 1×2 cm. anal margin	Squamous cell epithelioma, not graded	Supervoltage roentgen therapy anus, 1800 r; gold radon seeds into tumor 933 mc-hr.	Yes 4 yr.	No complaints
vii 1935	M	M	77	Multiple discharging fistulae 10 yr.	Large, fungating infected tumor 12×15cm. Large fixed nodes both groins	Squamous cell epithelioma, Grade 3	Supervoltage roentgen therapy: L. groin, 1800 r; R. groin, 1800 r; anus, 4200 r; radium-platinum needles, 1120 mg-hr.	No	Anal region cleared up. Died of general met- astasis in 6 mo.
VIII 1935	D	M	44	Tumor for 4 mo.	Tumor 10 ×10 cm., fungating and ulcerating, occluding the anus	Squamous cell epithelioma, Grade 1	(1) Colostomy (2) High voltage roentgen therapy, anus, 3000 r	Yes $3\frac{1}{2}$ yr.	Developed a ra- dionecrosis over the coccyx which was removed and area healed. Well otherwise
1X 1936	K	F	52	Rectal bleeding and backache 4 mo.	Tumor 3 ×4 cm. ant. wall, ex- tending into daginal septum	Squamous cell epithelioma, Grade 3	Supervoltage roentgen therapy:  4200 r anus 2700 r coccyx 1500 r  Radium-platinum needles interstitially, 1120 mg-hr.	Yes 3½ yr.	No complaints
x 1937	L	M col.	51	Bleeding I yr., backache	Tumor 3 ×4 cm. inside sphincter on anterior wall	Squamous cell epithelioma, Grade 3	Supervoltage roentgen therapy: anus, 1800 r; L. groin, 900 r; R. groin, 900 r; radium-platinum needles, 2230 mg-hr.	Yes I yr. but failing	Patient developed internal metastasis. Very weak. Will die soon*
x1 1938	Т	F	66	Bleeding I yr. and lump in anus	Tumor 3 ×3 cm. inside anus on posterior wall	Squamous cell epithelioma, Grade 4	Supervoltage roentgen therapy:  4200 r anus 2100 r coccyx 2100 r	Yes 1 yr.	No complaints
XII 1938	P	F	73	Bleeding I yr., moderate pain	Cauliflower lump 6 cm. diameter protruding from anus	Squamous cell epithelioma, Grade 4	Supervoltage   roentgen	Yes I yr. but failing	Tumor complete- ly disappeared then recurred and invaded ischio- rectal fossa. De- veloped metasta- sis internally*
XIII 1938	D	F	67	Bleeding 1 yr., pain in perineum	Mass 3×3 cm. in ant. wall, invading the perineum and vaginal septum	Squamous cell eptihelioma, Grade 3	Supervoltage roentgen therapy:  anus 3600 r sacrum and coccyx 1800 r L. groin 1500 r R. groin 1500 r Radium—contact. 2 mm. gold; intrarectal, 600 mg- hr.; intravaginal, 600 mg- hr.	Yes 10 mo.	No complaints

<sup>\*</sup> These patients have both died since the paper was read.

contact.

growth was on the mucous membrane side of the sphincters.

Pain was not a major symptom except late in the course of the disease and then only when the growth became so extensive that there was invasion of the deeper structures. Much of the pain was probably due to the accompanying secondary infection. An indefinite backache was present in 3 individuals, while only one had obstructive symptoms, though the anus seemed to be almost completely occluded in another.

How long the disease remains localized is difficult to answer. Given an area that is definitely and potentially infected—one that is constantly being compressed by the muscular contractions of both rectal sphincters—it would be only natural to expect dislodgment of tumor emboli into the lymph stream; however, these tumors are the fungating type and since they do not infitrate the base very early it is our impression that metastasis is rather late. Only 2 cases in this group had inguinal metastasis, while 2 others developed internal metastasis from one to two years after rectal bleeding first began. With such a Now natural course the outlook for successful treatment is favorable.

### DIAGNOSIS

The diagnosis is not difficult. The examining finger can readily reach and should differentiate the normal from the abnormal. Excluding a papillitis and a thrombosed hemorrhoid, the only confusing conditions are the granulations encountered around old fistulous tracts. These may be pyogenic, tuberculous or luetic, and, in all, the clinical impressions must be verified by biopsy.

### TREATMENT TECHNIQUE

All patients were treated by irradiation, but since the observation period extended over a fifteen year period, the technique as used varied considerably. The factors used were as follows:

### I. Roentgen Rays

- (a) 200 ky., 4 ma., 0.5 mm. Cu plus 1 mm. Al, 50 cm. distance, 0.16 Å.
- (b) 600 kv., 4 ma., 0.8 mm. Pb, 50 cm. distance, 0.044 Å.

### II. Radium

- (a) 50 mg., 1 mm. brass plus 1 mm. rubber filter
- (b) 50 mg., 2 mm. gold plus 2 mm. rubber filter
- (c) 1.3 to 2 mg. needles, filter 0.5 mm. platinum.
- (d) Radon seeds, filter 0.3 mm. gold.

Each case was individualized, the dosage varying according to the size of the lesion and histological structure. Usually roentgen therapy was given to the tumor through two portals: (a) the sacrococcygeal, (b) the anal or perineal. Treatment was given to the inguinal regions when metastases were already present or when metastases were suspected.

#### DISCUSSION

Since malignant disease of the anus is readily discovered by palpatory and visual examinations, it should be recognized early enough to be treated successfully either by surgery or irradiation. However, when radical surgery is the method of attack it has the disadvantage of removing or destroying the anal sphincters with subsequent loss of fecal control. On the other hand, when the operation is too conservative, local recurrence and inguinal metastases are prompt in their appearance. Since the tumors that have been graded have largely been either in Grade 3 or 4 of Broders' classification, one might expect recurrences.

Looking at the problem from a radiotherapeutic viewpoint, the great majority of these tumors are epitheliomata—types that have been successfully eradicated by irradiation in other parts of the body, so that the response here should be just as favorable. They are accessible and present little difficulty in administering an adequate tumor dose when treated by roentgen rays; while radium may easily be used in a contact applicator against the tumor, or interstitially in platinum needles or as radon in gold seeds. Except for one patient who had a very extensive growth practically occluding the anus, there was no need for any supplementary procedure, as a colostomy. The discomfort from the treatment is not great and is a matter of three or four weeks. The patients are ambulatory and usually are able to care for themselves. The sphincter control has been good except in 2 patients, in both of whom the sphincter was partly destroyed by the growth itself; one had a colostomy and the other now complains of discomfort from a partial stricture following the treatment. Finally, the effectiveness of irradiation is shown in the eradication of the carcinoma for varying periods of time, as seen below:

Total cases reviewed 13 Not treated I with advanced general metastasis at time of treatment Treated but dead. I moderately early who developed internal metastasis 2-7 years 1-5 years 1-4 years 2-3 years Living (but failing 9 I—I year gradually from internal metastasis) ı—ı year ı—less than a vear

Though this series is small, it corroborates the opinion of Binkley and Bowing, who, from an extensive experience, emphasize the superiority of irradiation to surgery around the anus. Even such prominent rectal surgeons as Lockhart-Mummery and Rankin, who advocate radical surgery for carcinoma of the rectum, admit that irradiation is the method of choice in the treatment of epithelioma of the anus. Whether one should use roentgen rays or radium, combined or singly, is a matter of individual opinion and experience. We have combined the two methods, using roentgen irradiation first and following it with radium according to the individual response and need of each patient.

### SUMMARY

Since cancer of the anus practically always belongs to the epithelioma group, its treatment by irradiation is the method of choice because:

- (a) Histologically, it represents a type that responds readily and effectively to irradiation.
- (b) The curability ranks on a par with surgery.
  - (c) The morbidity is low.
- (d) Physiologic sphinter control is retained except where the sphincter is already partly destroyed by the disease.\*



<sup>\*</sup>For discussion see page 725.

### SURFACE APPLICATIONS OF RADON IN RECTAL CANCER\*

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RADIUM and high voltage roentgen rays are of value in the treatment of rectal cancer. They may be used to advantage routinely in the inoperable stages of disease as a palliative method, and as a curative method in selected operable cases. The results to be obtained, in both the operable and inoperable groups, will depend largely upon the dose and technique of application. Due to variation in extent of the local disease at the time treatment is commenced, and variation in the grades of malignancy and radiosensitivity of rectal cancer, no uniform dose or technique of application is suitable for all cases.

The technique that has proved of greatest value in our clinic is the preliminary employment of external applications of radium or high voltage roentgen rays, supplemented by interstitial implantations or local surface applications of radon. External therapy exerts a favorable influence upon the tumor but this influence is not always sufficient, with the presentday technique, to provide the highest degree of palliation or to completely eradicate the disease. Gold filtered radon seeds, as a means of increasing the intensity of tumor dosage, were used routinely for many years; but during the past three years we have employed, in a number of cases, in place of interstitial applications, small daily surface doses of radon.

Treatment by local rectal applications of radium or radon is not a new method. It constituted one of the earliest attempts to influence rectal cancer by radium. The technique of application, in the early days, was rather inaccurate. Frequently, there was difficulty in placing the radium and retaining it in position. Doses were usually large, total doses being given in one, two or three large applications, at

short intervals. Little attention was devoted to protection of the uninvaded rectal mucosa. Such local applications, at times, produced a favorable effect upon the cancer, but were frequently followed by a severe prolonged local reaction, characterized by marked tenesmus, burning, etc., which caused many patients to refuse further treatment. However, because of the favorable effect produced by this method upon the tumor in certain instances, it was decided to again use local applications, but to employ a different technique, giving careful consideration to the details which previously had produced undesirable local reactions.

Different types of applicators were tried. The type which has proved most satisfactory to date is one fashioned after an electrically lighted proctoscope. These scopes or tubes are slightly heavier than the ordinary proctoscope, the thickness being one-sixteenth of an inch of brass, which acts as a filter for the radium. The diameters vary from 1.5 to 2.5 cm., and the length from 10.0 to 25.0 cm. These applicators have a movable shoulder which may be fastened with a thumb-screw, so that the length of the tube inserted into the rectum is varied in accordance with the requirements of the case. This type of applicator can be adequately placed over the tumor by direct vision and fastened in position. The holders that contain the radon are modified obturators which fit within the applicators. The number of radon tubes for a given case are placed in the center of the distal end of the holder. By placing the radon in the center of the diameter, it is kept at a certain distance from the tumor. This distance will vary with the diameter of the instrument. The greater the diameter, the greater the tar-

<sup>\*</sup> Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.

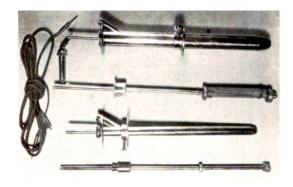


Fig. 1. Electrolighted rectal applicator and radium holders.

get distance and the greater the depth dose. Radon holders, in addition to containing radon, are fitted with lead shields to protect or provide additional filter for that part of the circumference of the rectum which is not invaded by cancer. Annular tumors do not require any shield. If the tumor involves less than one-third of the circumference a two-thirds shield is used. If less than one-half of the circumference is invaded, a shield of one-half size is used, etc.

Rectal applicator treatments are simple procedures and do not require hospitalization. Patients report for treatment daily. They are placed on a couch or bed in the left Sims' position. The applicator is inserted in a manner similar to that of passing an ordinary proctoscope. The instrument is passed above the tumor mass by direct vision, and then withdrawn so that the distal end of the scope is about 0.5 cm. above the upper limits. The radon holder, which previously has been loaded with the radon and the necessary shields, is inserted and fixed in position with a T-binder. The number of radon tubes placed in the holder will vary with the size of the tumor. These tubes, when arranged in tandem, should extend from 0.5 to 0.75 cm. above the upper limits of the tumor and the same distance below the lower limits of the mass. The length of radon in the holder may vary, therefore, from 3.0 to 12.0 cm. The time required for a treatment depends upon the amount of radon within the

applicator and the size of the daily dose to be administered.

Dosage. It was quite evident, after treating a few cases by daily applications in the above fashion, that if reactions were to be avoided the daily doses must be small. After trying various amounts, it was thought that doses varying from 150 to 250 mc-hr. were most suitable as they could be continued for a considerable time. The selected dose depends somewhat upon the number of radon tubes used in the applicator. A small tumor which can be accurately covered by two or three tubes will usually tolerate from 125 to 175 mc-hr. daily. More tubes and larger doses are required to deliver a similar tumor dose to all cells of a larger tumor. A radon tube is about 1.5 cm. in length, and the dose that has proved most satisfactory varies from 30 to 60 mc. for each tube, keeping the total daily dose somewhere between 150 and 250 mc-hr. Daily and total doses are governed also by the diameter of the applicator. When the applicator is small, 1.5 cm. or less in diameter, the daily dose should be smaller than when the large sized applicator of 2.5 cm. is employed. Bougies, large catheters and small applicators in stenosing lesions produce but little growth restraint and have not been found of much value. The larger the diameter of the applicator, the more effective is the treatment.

Total doses will depend largely upon the size of the tumor, the number of radon tubes, the diameter of the applicator, the radiosensitivity of the cells and the object of treatment, whether for palliation or complete eradication. In the case of the small early favorable radiosensitive cancers, when only two or three radon tubes are necessary, the required total dose may not be more than 2,500 to 3,000 mc-hr. given in daily doses of 150 mc-hr. Cancers of a slightly larger size, and those of a more radioresistant nature, may require 150, 200 or 250 mc-hr. daily until the dose of 5,000 to 6,000 mc-hr., or more has been delivered. Careful observation as to re-

action and response of the tumor to treatment is of value in determining the total dose. If the response is not satisfactory after a moderate dose has been administered to an operable case, it may be advisable to use radon seeds or subject the patient to radical surgical removal. Total doses employed in the inoperable group have been smaller than those used with the object of eradication. The object of treatment in this group is to provide palliation without any additional upset or reaction to the patient. Therefore, it is wise to keep the dose within the limits of that which produces even mild reaction. Small daily doses, continued for periods of ten to fourteen days (total of 1,500 to 2,500 mc-hr.), usually produce very gratifying preliminary results. Occasionally much larger doses may be employed to advantage. Small series of treatments may be repeated in order to keep the growth under control. Small doses of gamma rays appear to have a marked influence upon the surface of the tumor characterized by a decrease of ulceration and infection and promoting a moderate degree of scar tissue, accompanied by a lessening of the local symptoms and an improvement in the general condition. Too large a total dose tends to produce breaking down on the surface and an increase of symptoms.

Untoward reactions following small daily doses of radon will be practically nil provided the cases are suitable for this type of therapy and that adequate dosage is employed. There were rather severe reactions in 2 patients with large squamous lesions. These reactions were characterized by severe pain and sloughing of the mass. The total dose in each case was large. We had a few moderate reactions in the early days of treatment in the inoperable group, by attempting to obtain a very high degree of palliation. There were 2 mildly painful skin reactions following treatments of lesions which involved the lower rectum and anal canal. In these 2 cases such reactions might have been avoided by a more careful placing of the radium. There has

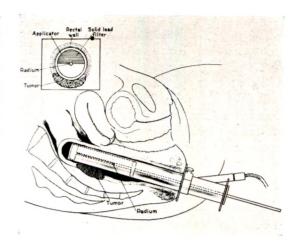


Fig. 2. Rectal applicator in position. Inset: Radium held in center of applicator, additional lead filter, one-half the diameter, to protect the normal mucosa.

been very little post-irradiation damage to the surrounding rectal mucosa. In the operable group, there remains a small amount of scar tissue at the site of the original tumor in a few cases but in the majority little remains to indicate the site of the primary lesion. There has not occurred any degree of stricture formation worthy of mention from treatment of the early lesions. The majority of patients with small operable tumors felt better as soon as they had received four or five applications. Undesirable reactions in the inoperable group have been practically nil except in a few early cases where the total dose was too large.

Results. One hundred and nineteen patients were treated by this method prior to July, 1938. We were able to follow 114 of these patients for a sufficient time to draw some conclusions as to the value of the method. Eighty-one had advanced or inoperable disease. Thirty-three were considered, in accordance with the extent of local disease, to be operable cases. Thirteen of the operable group received this form of therapy prior to radical surgical removal, while 20 were treated with the object of clinical cure by radiation therapy, or a high degree of palliation. A fair percentage of patients with operable lesions chosen

for applicator treatment were elderly or in poor physical condition and not considered ideal for surgery. All patients received high voltage roentgen rays in addition to applicator treatments. While sufficient time has not elapsed to draw definite conclusions as to the final results of this type of treatment, a survey of the cases treated nine months or more ago offers a basis for advocating the method and continuing its use.

Results in the Inoperable Group. In the inoperable group of cases there appears to be additional palliation provided, other than that usually obtained from external irradiation, in about 90 per cent of the cases. In 30 per cent of these cases, the additional growth restraint and lessening of symptoms was mild. There appeared to be a moderate degree of additional effect in about 25 per cent of the cases. In the remaining 35 per cent there was a marked palliative effect. A large percentage of the latter group was rendered free of symptoms for a time. In comparing these palliative results with those obtained from the use of weak gold radon seeds in similar cases, in the majority of patients there appears to be an advantage in the local applications. However, gold seeds are still being used in cases that appear unsuitable for applicator treatment.

Small daily surface doses as a preoperative method of irradiation has a limited field. The chief limitation of this method is that the deep areas of infiltrating cells show little response. However, in some cases, there was a marked reduction in the size of the mass and considerable lessening of its fixation. In reviewing the pathological reports of 13 cases operated upon, there was a wide variation in the effect produced upon these tumors. In 2 cases, no evidence of cancer could be found. One of these was

squamous cell and the other adenocarcinoma. Both cases had received very large total doses. In 8 tumors there were no recognizable changes that could be attributed to treatment. In the remaining 5 tumors the radiation changes varied a great deal.

The chief interest in this type of treatment has been with the small operable cancers, in an effort to provide clinical cures. The preliminary results in this small group are rather encouraging and suggest continuation of the method, but with careful selection of patients. Local applications have proved to be particularly suitable for the thin, small, radiosensitive lesions situated within the rectum proper or anal canal.

A review of the 20 operable cases treated by external irradiation and local applications, as a means of providing a high degree of palliation or complete eradication, shows the following results:

Two patients required operation, as the primary lesions failed to disappear. One patient, with a large, squamous cell cancer, has not been seen for six months, but is thought still to have the lesion. Local applications were supplemented with gold seeds in 2 cases. Both of these cases are considered clinical cures today. Two patients are dead. One, with squamous cell carcinoma, died with metastases to the liver but without local disease. The other patient was free of disease when last seen and the cause of death is unknown. One elderly woman has metastases to the liver. There was no local disease at her last visit. The remaining 12 patients, treated in the above manner, are alive and clinically free of disease for periods varying from one to three years.\*

<sup>\*</sup> For discussion see page 725.



# CARCINOMA OF THE COLON (EXCLUSIVE OF THE RECTUM)\*

By WILLIAM M. SHEDDEN, M.D., and RICHARD DRESSER, M.D. BOSTON, MASSACHUSETTS

CARCINOMA of the large bowel, excepting the rectum, is of course the most commonly encountered type of intestinal cancer. Most observers agree that the incidence of malignant degeneration of adenomatous polyps of the colon is approximately 50 per cent, though it has been stated to be as high as 85 per cent and as low as 18 per cent (Figs. 1, 2 and 3).

The reports vary with the histological interpretation of the polyp. Westhues has described an advanced change in these adenomas in which all order is lost. The branches, elongated tubules with cup-like outgrowths, the cells of which are many layered and deeply staining, have lost a definite relationship to the basement membrane. The muscularis mucosae is absent in many places and the connective tissue pedicle is sparse or absent. At the base of the lesion the gland tubules are distorted and pushed apart.

The papillomas comprise another gross

division of benign polypoid tumors, and in histological examination of these tumors it is of importance to examine the whole

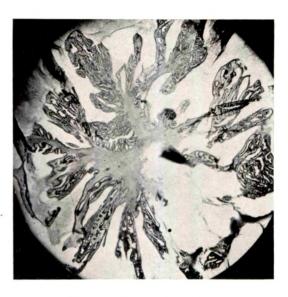


Fig. 1. Adenomatous polyp.

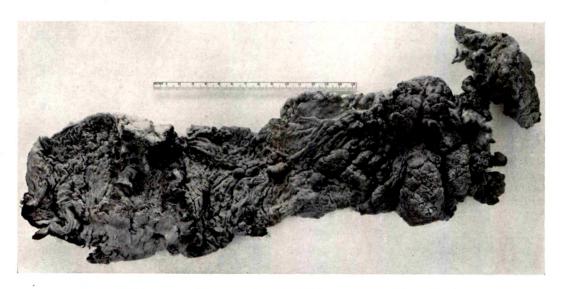


Fig. 2. Carcinoma at either end of a nest of adenomatous polyps. (Staff case, Palmer Memorial Hospital, courtesy of Dr. Richard Sweet.)

<sup>\*</sup> Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.

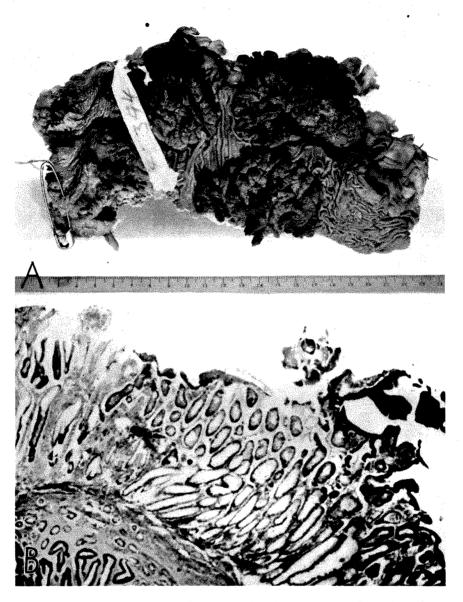


Fig. 3. A, two carcinomas of large bowel in close proximity, B, section of polyp which protruded from a colostomy.

tumor, as the base and center are most likely to show carcinomatous changes.

Multiple polyposis has an alarming tendency to carcinomatous degeneration. Several workers have demonstrated a gradual transition of polypoid growth from hyperplasia to adenoma with differentiated epithelial structure and then to less differentiated epithelial growths (Fig. 4).

It is not difficult to find instances of familial incidence of large bowel growths, both malignant and in the premalignant stage. As family histories are being more carefully investigated, an increasing number of instances of multiple polyposis, both with and without carcinomatous degeneration, are coming to light. This has been particularly noted in the literature of the past two or three years.

Both clinically and from the roentgen point of view, two definite types of growth

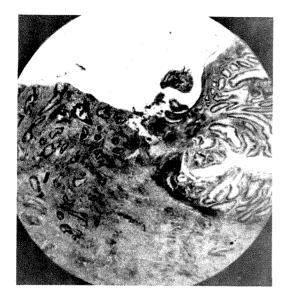


Fig. 4. Benign adenoma and adenocarcinoma in the same rectum.

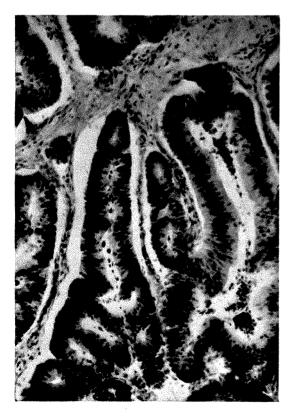


Fig. 5. Malignant adenoma.

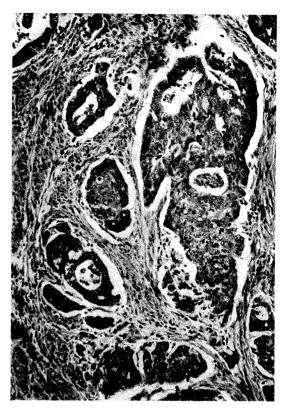


Fig. 6. Adenocarcinoma.

are recognized: (a) the medullary adenocarcinoma, commonly found in the ascending colon and at the hepatic flexure, and (b) the scirrhous obstructing type, usually seen in the remainder of the colon. This differentiation between medullary and scirrhous is often, however, only a gross one, for under the microscope the tumors of the two sides will many times not show this differentiation (Figs. 5, 6 and 7). Both have been found on either side of the colon, though the gross diagnosis in some instances of medullary or scirrhous carcinoma did not always coincide with the appearance under the microscope. Metastasis with carcinoma of the colon fortunately usually occurs late in the course of the disease. It must be remembered that enlarged hard regional nodes may not connote metastasis. We have in 2 cases recently resected a colon containing such nodes in the mesentery to find them entirely innocent of cancer.

#### SYMPTOMS

The symptoms are: (a) anemia, (b)intoxication, (c) obstruction.

Anemia: It is recognized that the medullary growths are friable and bleed easily. It has frequently been mentioned that the presence of this type of tumor in the right colon, that portion of the bowel which has a high capacity for absorption and where the fecal masses are still liquid, scopic, from the stools does not rule out cancer.

Obstruction: If obstruction supervenes, over three-quarters of the obstructing lesions will be found to be in the left half of the colon. While it is true that the right colon growth tends to grow in a centrifugal manner and is thus less likely to obstruct than its annular neighbor on the left, yet perhaps as good a reason for the tendency

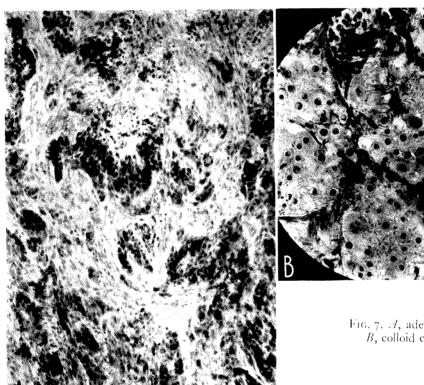


Fig. 7. A, adenocarcinoma; B, colloid carcinoma.

is a probable reason for the anemia and intoxication that are frequently seen in these cases. However, it is sometimes hard to explain the marked anemia and intoxication in cases with relatively small lesions. Recent studies have been made4 of the intestine proximal to carcinoma of the right side of the colon, but no changes were noted in the anatomical structure of the intestine which might account for the associated anemia, on the basis of absorption of perverted substances. Obviously, absence of blood, either gross or microto bowel stoppage on the left is the diameter of the distal colon, which may normally be as small as 2.5 cm., as against 7.5 cm. on the right.

Fortunately these obstructive symptoms will often appear fairly early, but there is always the danger that the patient or the doctor will be misled by the disappearance of the vague slight symptoms of early obstruction after a change to a low residue diet or the ingestion of oil (Fig. 8). At the present writing, obstruction is being recognized clinically in about 50 per cent of the cases. In about 5 per cent of these the obstruction is acute.

With the pressure of cancer publicity on both patient and doctor, more early cases are appearing. It is impressive to note the insignificance of the symptoms in these early cases. The patient may be so undisturbed by them that he only recalls them with an effort and often close questioning by the examiner. Only too often is it discovered that a minimal change in bowel habit, an insignificant digestive disturbance, a slight anemia or a vague slight general weakness indicate a process already quite advanced. There are still many carcinomas of the colon discovered first at autopsy.

The ideal situation would be, of course, one in which a carcinoma of the colon was treated before it had developed far enough to produce symptoms. Without question the more frequent employment of the barium enema as part of a routine physical examination will bring us nearer to attaining this end. As the barium enema examination becomes less expensive, more early cases will be discovered. We must keep always in mind that there are no pathognomonic symptoms of carcinoma of the large bowel.

Ten years ago we operated upon a carcinoma of the descending colon. In the eighth year following operation, the patient developed symptoms of pulmonary pathology which was diagnosed by the roentgen ray as carcinoma. But it was only at autopsy that the primary focus was discovered to be in the colon well above the level of previous resection—undiagnosed, for it gave no symptoms.

### ROENTGENOLOGIC EXAMINATION

It is being increasingly emphasized that negative findings are of no significance, and there is a gratifying increase in accuracy in locating growths proximal to the sigmoidal flexure—in some series it is as high as 98 per cent. It is recognized that the opaque enema is not infallible and that lesions of the large intestine occasionally

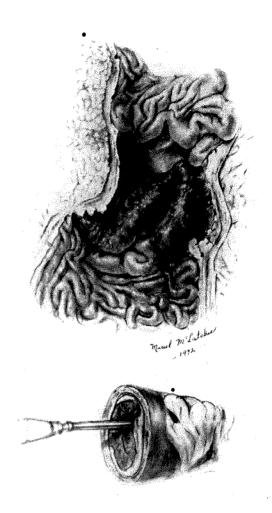


Fig. 8. Stricturing carcinoma. Symptoms relieved by injection of oil.

are present which give no roentgen evidence of their existence (Fig. 9). The contrast enema usually reveals those carcinomas which encircle the gut and produce some degree of stenosis. If, however, there is no constriction of the colon, the diagnosis may become difficult. The study of the mucosal pattern after evacuation of the contrast enema is of great importance and should be carried out in all cases, though the examination of the mucous membrane of the colon has not yet reached the degree of perfection that it has with gastric lesions. The combination of air insufflation and contrast enema is occasionally helpful, although of course it is

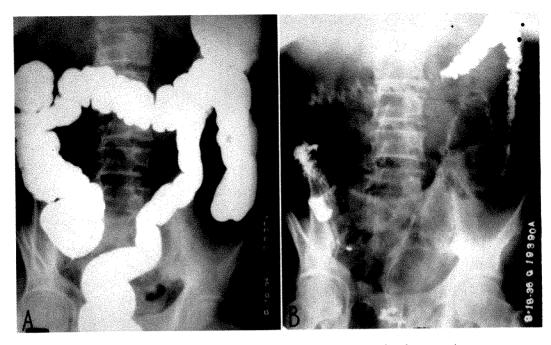


Fig. 9. A, carcinoma of the large bowel, roentgen examination negative after barium enema; B, after evacuation of barium.

not necessary to employ this method routinely. Care must be exercised in examining the flexures of the colon where overlapping loops are likely to obscure even well-advanced lesions (Figs. 10 and 11).

### TREATMENT-SURGICAL

With cancer of the colon, particularly the right colon, the prospects of cure are



Fig. 10. Loop of sigmoid conceals carcinoma proximal to it.

usually better than with the stomach, as the lymphatic circulation is not so abundant. In the presence of obstruction, the ileus must obviously be treated first (Fig. 12). Preliminary colostomy markedly lessens the primary operative mortality. For removal of the tumor, four surgical methods are available:

(1) Excision of the growth with immediate anastomosis, preceded by several

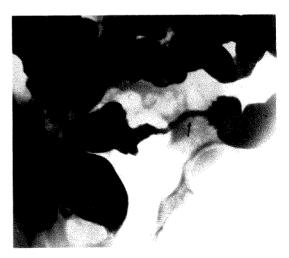


Fig. 11. Same patient as in Figure 10. Carcinoma of sigmoid revealed by pushing loop to one side.

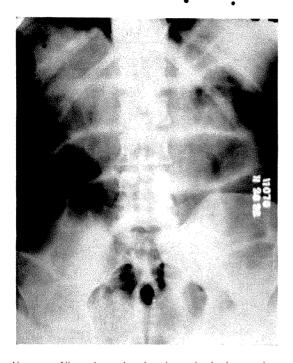


Fig. 12. Flat plate showing intestinal obstruction. days by a colostomy proximal to the

growth. The following case history is illustrative.

W. K. S., aged fifty-seven, entered the hos-

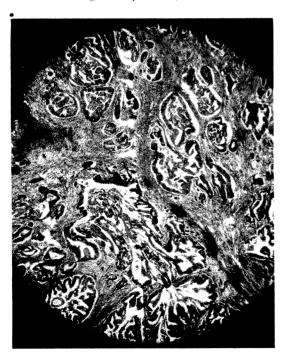


Fig. 13. Carcinoma of the hepatic flexure

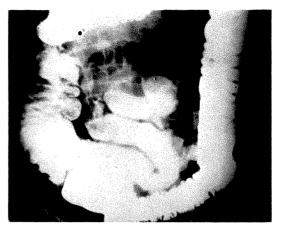


Fig. 14. Obstructing carcinoma of hepatic flexure.

pital complaining of severe cramping lower abdominal pain. Duration three hours. Patient had had two similar attacks one month previously but they were so mild that he had thought nothing of them. Had no constipation in the interval between attacks. Barium enema quite negative and he was discharged. Ten days later he returned with a definite acute intestinal obstruction. An immediate cecostomy was done. Twelve days later the right colon was resected and an end-to-side anastomosis of the ileum to the hepatic flexure was performed. His recovery was uneventful.

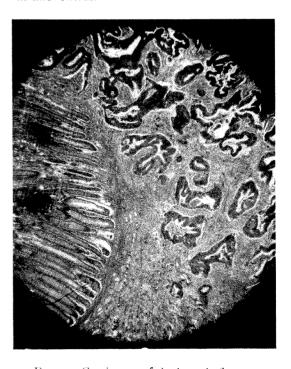


Fig. 15. Carcinoma of the hepatic flexure.

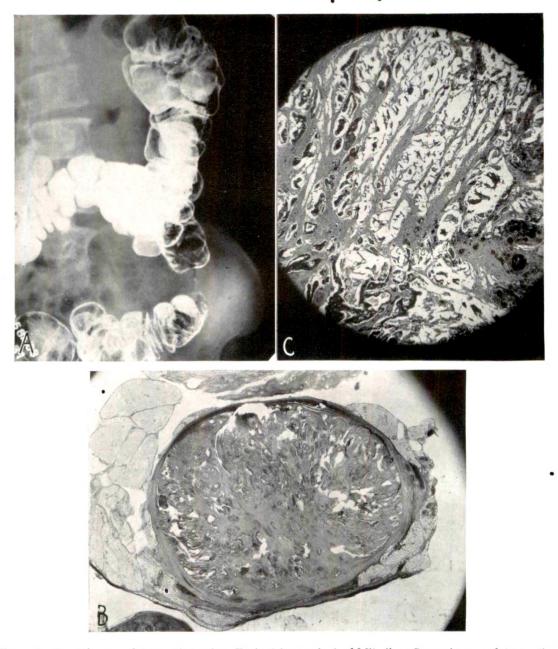


Fig. 16. A, carcinoma of descending colon. Excised by method of Mikulicz; B, carcinoma of descending colon. Node in mesentery; C, photomicrograph of section of carcinoma of descending colon.

Comment. Despite lack of constipation between attacks and a negative barium enema this patient had a constricting carcinoma of the hepatic flexure (Fig. 13).

(2) Preliminary anastomosis with secondary removal of the growth (in cases without obstruction) (Figs. 14 and 15). The following case history is illustrative.

W. W. G., aged sixty-seven, stated that one year and again six months before entrance he had a short attack of frequent loose stools without other symptoms. Between attacks bowels were quite regular. Began to lose weight three months before entrance and lost 7 pounds during that period. Appetite became poor during the same period. One week before entrance vomited and abdomen became distended, but

following this he had good results from an enenta. He quieted down. This recurred the day before entrance. A cecostomy was done to relieve the obstruction. A barium enema showed a carcinoma of the hepatic flexure. Ten days later an ileo-transverse colostomy was performed. Two weeks later a right colectomy was done, including the cecum. No nodes were involved. The area of the cecostomy was drained. During convalescence a small superficial abscess was evacuated from the wound. Convalescence otherwise was uneventful.

Comment. Slow-growing carcinoma which probably could have been discovered several months earlier.

- (3) Preliminary colostomy with secondary enterectomy followed eventually by closure of the colostomy. The following case history is illustrative.
- J. B. McG., aged 65, entered the hospital because the constipation which he had noted for the past year had become more severe. He had no other symptoms. Barium enema showed an obstructing lesion in the descending colon. Operation: A transverse colostomy (at the proximal end of the transverse colon) was performed. His bowel distal to this point was well cleaned out during the next two weeks. A second operation was then performed. The involved descending colon with a goodly amount of accompanying mesentery was resected. Several large hard nodes in this mesentery were found to be merely inflammatory. At a third operation the colostomy was closed.

Comment. A preliminary colostomy was done because of beginning obstruction. A resection of a goodly amount of mesentery was performed because of palpable local nodes.

(4) The method of Mikulicz (Fig. 16A, B and C). The objection to this method is in the definite danger of transplantation of tumor cells into the abdominal incision. As high as 12 per cent has been reported. The obstructive resection of Rankin, when feasible, is a better operation. The operative mortality averaged over a number of series will be about 30 per cent. The mortality for lesions on the left side is always about 10 per cent higher than that with lesions of the right colon. The total

mortality can be and has been brought as low as 12 per cent in large series. The following is an illustrative case history:

G. C., aged forty-five, stated that six months before entrance he had cramps just below the umbilicus. He was relieved as soon as gas was passed. Relieved by evacuation of bowels. No relation to meals. Has always been constipated, but with the use of oil and psyllium seeds his bowels became regular. No melena. No diarrhea. No loss of weight. At that time abdominal examination negative. An entrance examination revealed a mass, 6 cm. in diameter, along left flank at level of anterior spine of ilium. Barium enema showed an obstructive lesion of the descending colon. Resection (first-stage Mikulicz). Patient was then sent home for a month. During this time the spur softened and became more attenuated. At the end of a month the spur was crushed. One month later the colostomy was closed. Convalescence uneventful.

Comment. Inasmuch as at entrance the patient had a palpable fixed mass, it seemed questionably operable. However, resection was successful. Although nodes containing cancer were found in the mesentery, he has been well for over three years.

#### END-RESULTS

One should be able to attain approximately 50 per cent of three year arrests but about one-quarter of these will recur after five years. However, Dixon has reported 55 per cent five year arrests with carcinoma of the cecum. The prognosis of carcinoma of the colon is increasingly less favorable as the more distal segments of the colon are involved. Lymphatic spread of right colon carcinoma commonly involves nodes in close proximity to the bowel. Resection of the affected segment, therefore, necessarily permits the removal of the accompanying lymphatic structures. The operability of carcinomas of the colon at the present writing is about 60 per cent.

The importance of obtaining material for microscopic examination either through a sigmoidoscope or a laparotomy cannot be overemphasized. The consequences which may follow such an omission were forcibly brought to our attention a number of years ago in the case of a middle-aged man who developed symptoms of progressive intestinal obstruction. He was examined by barium enema and a complete arrest of the enema was noted at the rectosigmoid junction. Exploratory laparotomy showed a large, firm mass involving the sigmoid which it was considered impossible to remove surgically. The patient was referred with a diagnosis of hopeless carcinoma. The obstructive symptoms had been relieved by cecostomy. Subsequent proctoscopic and roentgen investigations finally suggested that the mass was the result of diverticulitis. The patient was again explored and a permanent low leftsided colostomy was done. Seven years have elapsed and the patient is leading a normal existence, is in perfect health, and presents no evidence of malignant disease.

#### TREATMENT—RADIATION

The treatment of carcinoma of the large intestine with 200 kv. roentgen ravs has given such discouraging results that we have practically discontinued this type of therapy. With the advent of supervoltage roentgen rays, however, it was felt that irradiation of malignant neoplasms of the colon should be resumed. Thus far, only a small group has been treated, consisting of 13 cases, 6 being low enough for sigmoidoscopic investigation. The entire group was hopeless from the surgical standpoint. These patients have been treated with the electrostatic belt-conveyor apparatus described in earlier communications. The following factors have been employed: 1,000,000 volts constant potential; 70 cm. distance; 3.5 mm. lead and 7 mm. copper filter; half-value layer 10.5 mm. copper; 70 r per minute, thimble-chamber air measurement. The daily doses ranged from 200 to 400 r, with total doses running as high as 6,000 r. We have been impressed with the tolerance which these patients have shown for supervoltage roentgen rays. Roentgen sickness has been definitely less

than at lower voltages, and skin reactions have been negligible.

Radiation was administered as a palliative rather than a curative measure. These cases experienced relief from pain and diminution of bleeding. In several instances there was marked regression in the size of the growth. Two cases may be cited as examples:

A man, aged thirty-six, came under our observation a year ago with multiple large abdominal masses arising from a primary carcinoma of the sigmoid. The patient received two courses of supervoltage radiation, and at present there is no palpable evidence of disease other than slight thickening in the left lower quadrant. He is now symptom free.

The second case is that of a male, aged sixty-four, who in June, 1938, was found to have a carcinoma of the sigmoid which caused complete obstruction. A colostomy was performed. This patient has had five courses of supervoltage radiation with the result that a proctoscope now can be passed easily beyond the previously constricted area with no sign of ulceration or bleeding.

We appreciate that this group of cases of advanced, inoperable cancer has not been treated with any great enthusiasm and it seems likely that larger doses, which we have discovered are entirely safe to give, may lead to improved results.

#### SUMMARY AND CONCLUSIONS

- 1. Carcinoma of the colon is commonly encountered.
- 2. More early cases will be discovered if it is realized that they have no pathognomonic symptoms.
- 3. The benign adenoma, precursor of the malignant adenoma, must be diligently searched for, and destroyed.
- 4. A negative roentgen examination after a barium enema does not, of course, rule out carcinoma.
- 5. Resection of the involved bowel, preferably by stage operations, is the treatment of choice.
- 6. Palliation can occasionally be obtained with supervoltage radiation.

#### REFERENCES

1. Dixon, C. F. Carcinoma of right half of colon; diagnosis and treatment. New York State J. Med., 1938, 38, 1262-1265.

 Dresser, R., Trump, John, and Van de Graaff, R. J. Production of supervoltage roentgen rays by means of an electrostatic generator. Am. J. Roentgenol. & Rad. Therapy, 1937, 38, 758-761.

3. TRUMP, J. G., and VAN DE GRAAFF, R. J. Design of a million volt x-ray generator for cancer treatment and research. J. Applied Physics, 1937, 8, 602-606.

4. Welch, C. S., Mayo, C. W., and Wakefield, E. G. Histologic study of intestine proximal to carcinoma of right side of colon, associated with anemia. Surgery, 1937, 2, 849-851.

 Westhues, H. Die pathologisch-anatomischen Grundlagen der Chirurgie des Rectumkarzinoms. Georg Thieme, Leipzig, 1934.

#### DISCUSSION ON PAPERS OF DRS. MELAND, BINKLEY, AND SHEDDEN AND DRESSER

Dr. L. R. Sante, St. Louis, Mo. The question of anal, rectal and colon carcinoma again seems to me to revert to the question of type of cell and its radiosensitivity and the relative resistance of the normal surrounding tissue cells in which it is embedded. Frankly, the tumors in which we have had our success have been the ones in which there was the epidermoid type of carcinoma of the anus, and those that spread from posterior lip carcinoma of the cervix to involve the rectum.

It is obvious that since we do have success in those cases and have fewer successes in the adenocarcinoma types (the resistant cell types, which arise primarily from the rectum), this must be a matter, not so much of technique as the actual sensitivity of the cell.

I think rectal carcinoma is a bugbear for most of us and the matter of application is of course also of great importance. In this new applicator device as shown this morning it seems we have something very good. I think that in the past those of us engaged in general radiology and treatment have been rather remiss in our treatment of carcinoma of the rectum, feeling that there is nothing much we can do anyway, and we have by a more or less hit-or-miss method applied a rectal applicator, perhaps made up with radium tubes in an ordinary colon tube; or if the lesion were on one side, with one of the old-style fenestrated lead applicators with the radium in direct application to the tumor—

with all of the lead on the opposite side for protection.

It seems to me the cylindrical applicator which allows for the increased distance is a great advantage. The application in this manner, of course, gives a greater depth dose and makes it easy to put in time after time.

I think the carrying of this matter of fractional dose radiation for the use of radium in rectal carcinoma and in the resistant type of cell structure is a very great advantage and it is a procedure that we should carry out with more exactitude and more frequently. It is a little bit difficult and it is quite a lot of inconvenience to get a patient up day after day and make a daily application of small doses of radium—it is quite a task, and I am afraid that many of us, on account of the disagreeableness of the task and the feeling of pessimism have not, perhaps, carried it out faithfully and given it the full amount of attention that we should.

I think that this applicator is certainly a great step in advance and it seems to me that it offers opportunities for different placement of radium rather than just the center of the applicator, because after all, this is not always the best or most advantageous arrangement for the radium.

In the use of seeds, it has always been very difficult for us to be sure that we are making any kind of a logical distribution of seeds in rectal carcinoma. Very frankly, it sounds easy, but when you look through a very small tube and there is a carcinoma high up and you see only the proximal end (it isn't always easy to visualize the other end to determine how far it extends), and above all you do not have the advantage of palpation, it is actually a very difficult thing to do.

Another troublesome complication which sometimes occurs and which leaves us fearful is the advent of a complication of perirectal abscess. I am sure that you have all had this condition develop after application of seeds at some time; it is an experience which causes one to err on the conservative side, in subsequent cases, resulting at times in insufficient irradiation of the growth.

I think utilization of the applicators that have been devised with careful thought in the individual case, maintaining the applicator in proper place, and the use of the fractional dose method, offer considerable advance in our treatment of carcinoma in this location.

In the matter of carcinoma of the colon, it seems to me that this is definitely the realm of surgery and our main function, if I may be permitted to say just a word in discussion of the paper that mentioned it, is in the early diagnosis of the lesion because in this place in the gastrointestinal tract there is an opportunity for early surgery to give very satisfactory results.

The insidiousness with which carcinoma hides around the bends of the colon was graphically demonstrated this morning, and how it is necessary to rotate the patient so as to uncover these bends in the rectosigmoid juncture, the hepatic and splenic flexures. If the constriction of the carcinoma is annular, the proximal dilatation of the colon—even if it is just a relative dilatation—and the distal constriction in itself points to the location of the lesion. But if it is pedunculated, springing from one wall so that it doesn't completely constrict the colon, then there is no dilatation above and the difficulty is greatly increased. It seems to me that we can help do our part by making an early diagnosis and being meticulous in our examination.

The application of roentgen therapy to such growths that may be large and inaccessible is of course just a palliative effort; we cannot view it with too great hope. If there is a colostomy with the colonic mucosa right next to the skin, both included in the roentgen field, and if the customary doses of radiation are given, you will see that very soon, before the skin shows any evidence of reaction, the intestinal mucosa will become definitely red, bleed, and will show a pseudo-membrane, and by the time actual reddening of the skin occurs there are already ulcerations of the colonic mucosa. This should in itself point out to us that the mucosa of the bowel is distinctly sensitive so that when it is involved with a carcinoma that is many times more resistant than the normal intestinal mucosa itself, we can have little hope of destroying the carcinoma without destroying the intestinal mucosa also. Therein lies the limitations of radiation therapy in the abdomen: the sensitiveness of the surrounding normal structures.

DR. ROBERT E. FRICKE, Rochester, Minn. It was my privilege last fall, at the meeting of the American Roentgen Ray Society, to hear and discuss Dr. Kaplan's paper on carcinoma of the anus. I believe the consensus at that time was that fortunately the incidence of this type of growth is rare and the treatment has to be highly individualized. The involved region is very

tender both in regard to treatment and as regards the later reaction from the treatment. Although the primary growth "melts down" very swiftly and beautifully with treatment, and usually is a Grade 3 or 4 squamous cell epithelioma, the prognosis is always bad on account of the probability of later general metastasis.

Commenting on Dr. Binkley's paper, we have been using the surface treatment at the Mayo Clinic for many years, although our technique is a little different. We use two radon tubes strapped together, 50 or 60 mc. in each, introduced through a proctoscope with the patient on a Buie table and treat the different regions daily.

There are two groups of cases. In the larger group the treatment is only palliative as the patients already have metastases to the liver or lungs; one desires to control the distressing rectal symptoms and the dose is necessarily small. We give over each area about 50 to 100 mc-hr. per square centimeter a day until the lesion has been covered.

The other smaller group is made up of cases in which the lesion is operable. I believe there is quite a future for preoperative use of radium in these hopeful cases. Only a few are seen each year in our department. One year especially we studied results in a few cases in which radium therapy was used following colostomy in most cases during the convalescence from the colostomy. We treated the patients quite vigorously, and if we could get the surgeon to have patience for two or three months until the effect of treatment and the reaction from the treatment had been obtained, the subsequent posterior resection usually has been easier, the growths have practically always diminished in size and in 3 cases observed in one year there were no residual carcinoma cells found in the tissue removed at resection.

Dr. Meland (closing). I just wish to emphasize the fact that most of these patients that have epitheliomas of the anus are old patients. Even though they are technically operable, the surgical risk is great. Furthermore, those patients on whom we have done biopsies fall into the higher grades of malignancy, namely Grades 3 and 4. In irradiation we have a method of treatment that not only gives a high rate of curability but does not carry the mortality of radical surgery; while at the same time it preserves sphincter control.

being inside the terminal. The electrons originate from a flat spiral tungsten filament at the high voltage end, and are progressively accelerated and focused as they pass down the tube by the multiple electrostatic lens system which derives its potential distribution from the column. At the grounded end this stream of electrons passes through a thin aluminum window and emerges from vacuum into air as a beam of electrons homogeneous in energy.

# EFFECT OF HOMOGENEOUS AND PARALLEL CATHODE-RAY BEAM ON WOOD

When a beam of cathode rays, in which every electron has closely the same energy and direction as every other electron, is incident upon a block of wood, a qualitative impression of the distribution of the ionization energy within this material can be obtained from the charring effect produced. Figure 2 shows a section through a wood block after bombardment by a 1,500 kv. electron beam. It is seen that the zone of maximum energy absorption, or ionization, lies well below the surface, and that no evidence of ionization exists beyond a certain maximum depth which might be termed the range of electrons of this energy. The dosage which produced the charring effect in this sample of wood was approximately a thousand times a therapeutic dose. The time required to produce this charring effect could be selected at will by regulating the current in the beam. The time of irradiation can easily be made as long as several minutes in order to permit an accurate control of the dosage. The total amount of electric charge which is incident upon the material can be measured by the simple expedient of connecting an electrometer between it and ground.

# DISTRIBUTION OF IONIZATION WITHIN VARIOUS ABSORBERS

Using the cathode-ray source described above, a study was made of the ionization produced by high speed electrons in their passage through lead, copper, aluminum, and water. The distribution of ionization in water is of special interest herein because of its close correspondence to tissue. The ionization was produced within a thin chamber mounted closely below the aluminum cathode-ray window. The electrodes of this ionization chamber, which is shown in Figure 3, consisted of a 0.0006 inch stretched aluminum diaphragm, insulated and separated by 0.030 inch from a heavy steel disk. By inserting between the cathode-ray window and this ionization cham-

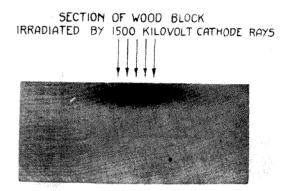


Fig. 2. Qualitative evidence of the distribution of the energy of a 1,500 kv. cathode-ray beam below the surface of a wooden block.

ber thin sheets of the material studied, the chamber could in effect be placed at varying distances below the surface of these materials and the ionization at these levels determined. For convenience, the material of the lower electrode of the ionization chamber was not changed to correspond to the absorber material, though this would be expected to have some effect on back-scattering.

Measurements were made of the total electron current incident on the material, and of the ionization produced within the chamber for various positions below the absorber surface. The ratio of this ionization current to the incident electron beam current as a function of the thickness of the material interposed in the path of the cathode-ray beam is given in Figures 4 to 7 for lead, copper, aluminum and water,

respectively. These measurements were made with cathode rays incident with 300, 500, 900, 1,100, 1,300, and 1,500 kv. of energy. The minimum thickness interposed was in all cases the thickness of the cathode-ray window plus that of the ionization chamber diaphragm, and totaled 0.0025 inch of aluminum.

It is seen from the curves that for the cathode rays of higher energy the ioniza-

ionization density falls steadily to a negligible value, indicating that the perceptible ionization effects are confined within the range of the electrons. This shows, as may be expected, that the roentgen rays produced by the cathode rays have no appreciable effect on the ionization density.

The range or maximum penetration of the cathode rays in the various absorber

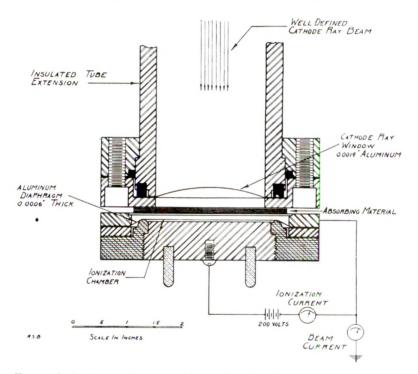


Fig. 3. Cathode-ray window and ionization chamber arrangement for the distribution of ionization measurements.

tion at this closest position to the surface of the absorber is about 60 per cent of the maximum ionization. Examination of these curves also shows that the relative distance below the surface of the absorber material at which the ionization is a maximum is greater for materials of low atomic number—such as water—than for those of high atomic number. This characteristic, which is probably due to the effect of nuclear scattering, which increases with atomic number, is favorable to cathode-ray therapy, since tissue is composed primarily of elements of low number. The curves show that beyond the peak the

materials may be taken as the end points of the curves in Figures 4 to 7. The range in water has been plotted in Figure 8 against the incident energy in kilovolts. This curve shows a substantially linear increase in penetration with the voltage except at the lower values.

# RADIATION THERAPY WITH CATHODE RAYS

The attractiveness of cathode rays for therapy lies in the fact that an ionization dose of therapeutic intensity can be applied to tissue in a fairly well localized region with only a fraction of the maximum intensity at the skin and a negligible amount of ionization beyond the welldefined cathode-ray range. This is in marked contrast to the distribution of iorization found in roentgen therapy, in which ionization is maximum at the skin and proceeds to diminish in accordance with the absorption and inverse-square laws. Figure 9 compares the distribution of ionization produced by a parallel beam of 1,500 kv. electrons with that produced by a 100 kv. roentgen-ray beam used with a 20 cm. target-to-skin distance and I mm. aluminum filtration. The intensity of ionization at the skin is set to be the same in both cases. It is to be noted that more than 95 per cent of the total ionization produced by the cathode-ray beam lies within 7 mm. of the skin, though the maximum intensity is found well below the skin. With the roentgen-ray beam, on the other hand, though the intensity is highest at the skin, only about 12 per cent of the total ionization lies within the first 7 mm., the balance occurring in the underlying tissues. For superficial malignant neoplasms within the range of cathode rays, the enormously greater effectiveness with which the ionization can be applied with cathode rays may prove a factor of prime importance. In certain cases it may prove desirable to use roentgen rays and cathode rays in combination to secure the most favorable distribution of ionization.

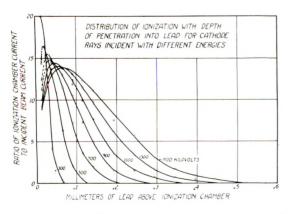


Fig. 4. Distribution of ionization with depth of penetration into lead for cathode rays incident with different energies.

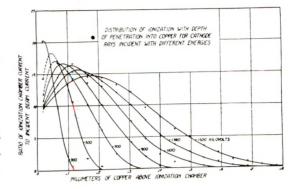


Fig. 5. Distribution of ionization with depth of penetration into copper for cathode rays incident with different energies.

The present unavailability of cathoderay sources for radiation therapy is due largely to the low range in tissue of even very high energy electrons. Only recently, using the highest constant potentials available, has the range of cathode rays become sufficient for the treatment of even very superficial malignant neoplasms. Fifteen hundred kilovolt cathode rays, as shown in Figure 8, have a maximum penetration of only about 7 mm. in tissue or water. Within this range is exhibited, however, the unique, localized distribution of ionization, the lack of which is one of the fundamentals limitations of roentgen therapy. For comparison with the 1,500 kv. cathode rays, the roentgen-ray voltage and

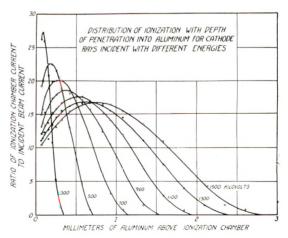


Fig. 6. Distribution of ionization with depth of penetration into aluminum for cathode rays incident with different energies.

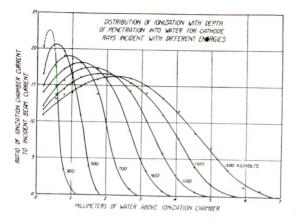


Fig. 7. Distribution of ionization with depth of penetration into water for cathode rays incident with different energies.

treatment distance used in Figure 9 was that typical of superficial roentgen treatment. Since the penetration of cathode rays increases directly with the accelerating voltage, developments now under way on the production of higher voltage sources may be expected to extend the present cathode-ray range several times. In the next few years, controlled beams of cathode rays homogeneous in energy and capable of penetrating several centimeters

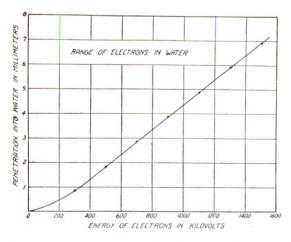


Fig. 8. Maximum range of cathode-ray beams in water as a function of their energy.

below the skin will probably become available for malignant growths within this range.

# REQUIREMENTS FOR CATHODE RAYS USEFUL FOR THERAPY

The particular property of cathode rays which renders them of interest in radiation therapy lies in their manner of absorption, which permits the placing of well-localized dosages below the skin. This absorption characteristic is due to the fact that the individual electrons, like other high energy charged particles, produce their maximum ionization near the end of their path. Though the ionization is a maximum near the end of the path of individual electrons, the effect of scattering on a parallel beam of electrons homogeneous in energy is to

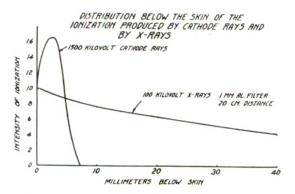


Fig. 9. Experimental curves showing the distribution in material similar to tissue of the ionization produced by 1,500 kv. cathode rays and by 100 kv. roentgen rays.

move the region of maximum ionization nearer the surface. This is due, in part, to the fact that many of the electrons are deflected from the straight course within the absorber and hence have their maximum ionizing power nearer the surface. The effect of cathode rays not homogeneous in energy, but containing many particles of lower-than-the-maximum voltage, would similarly tend to bring the maximum intensity of ionization nearer the surface. The absorption curve for such cathode rays would not have, to nearly the same extent, the desirable characteristics of the curve illustrated in Figure 9. Hence it may be stated that the principal requirements of cathode-ray therapy, assuming sufficient penetration, are that the rays be incident in a parallel beam essentially homogeneous in energy in order that the zone of maximum ionization may be localized and below the skin, and that the current in the cathode-ray beam be controllable so that the intensity of ionization may be of the same order of magnitude as that produced by roentgen rays in cancer therapy.

These requirements are not met by beta rays, which are not available in homogeneous or parallel beams of biologically useful intensity. Beta-ray emission from radioactive substances, as is well known, occurs with equal probability in all directions, and the distribution of energy among the emitted particles shows both a continuous and a line spectrum, with the lower energies predominating. The distribution of ionization about the beta-ray emitter, therefore, is strongly influenced by the inverse-square law and in addition shows high absorption immediately adjacent to the emitter surface. The net result is a region close to the emitter in which the radiation is excessive, beyond which the radiation rapidly diminishes to negligible proportions. This lack of control over the direction, energy distribution, and range of beta particles accounts for their disuse in radiation therapy.

The above requirements are also difficult to meet with cathode rays when a surge or a-c high voltage source is employed, due to the varying voltage and hence varying energies of the accelerated electrons, and also due to the lack of precise control of the electron current. With the constant potential electrostatic voltage source used in this investigation the voltage variation was of the order of I per cent, and the current in the cathode-ray beam could be regulated from a milliampere, which is used in roentgen-ray applications, to a very small fraction of a microampere. which would be desired for cathode-ray therapy. The particles in the cathode-ray beam could be sufficiently uniformly distributed over the desired area by placing a suitable seatterer some distance above the absorbing material and confining the beams by means of diaphragms to the area to be irradiated.

#### INTENSITY NEEDED IN CATHODE-RAY THERAPY

Because of the directness of the cathoderay process, less than one hundredth of I per cent of the current used in supervoltage roentgen therapy would be sufficient in cathode-ray therapy to produce comparable ionization intensities in tissue. In therapy with a million volt roentgen-ray generator4 operating at about I milliampere, for example, the energy of the electron beam is converted into roentgen radiation at the target with an efficiency of a few per cent. Of this radiation about I per cent passes through the roentgen-ray portal toward the patient. The ionization directed at the patient represents, therefore, a few hundredths of t per cent of the energy in the electron beam, and of this only a small fraction is absorbed within the tumor. In cathode-ray therapy, on the other hand, all of the electron energy within the prescribed beam area would be incident on the patient, and its effect would be localized within the limited range of the electrons. In order to produce within this localized region an ionization by cathode rays which is comparable in intensity to the ionization produced by roentgen rays in a typical treatment, the cathode-ray current should thus be less than one-tenth of a microampere. Such a controlled beam current, which is easily obtained with a constant potential voltage source, could be expected to produce its therapeutic effect at substantially the same rate as that now observed with roentgen rays. Since in roentgen therapy the therapeutic agents are the secondary electrons accelerated by the absorbed and scattered roentgen-ray quanta within the tissue, it is evident that the biological effect would in both types of therapy be due to moving electrons.

It is one of the advantages of homogeneous and parallel cathode-ray beams such as would be used in therapy that they can be described in a more simple and exact manner than roentgen-ray beams. Such incident cathode radiation is described by specifying the voltage, current, and treatment area. The character of an incident roentgen-ray beam, on the other hand, depends in addition to these factors on the wave form, target material, filtration, radiation angle, and treatment dis-

#### RANGE OF CATHODE RAYS IN TISSUE

With the 1,500 kv. cathode rays obtained with the present apparatus, the maximum range in water—and therefore in tissue—is about 7 millimeters. This present range is sufficient for exploring some of the biological effects of cathode rays and may later prove of medical interest in the treatment of certain types of very superficial malignant conditions. While many of these can already be effectively treated with roentgen rays, except when the involved area is large, the advantage of lower skin damage, of the higher intensity at the inner region of the malignant neoplasm, and of the absence of destructive action beyond the well-defined range of the electrons may prove significant. It is to be expected also that in the future substantial voltage increases will be made so that the penetration of cathode rays can be gradually extended to more deep-seated malignant tumors.

The authors take pleasure in expressing their appreciation of the generous grant of the Godfrey M. Hyams Trust which made possible the development of the pressure-insulated roentgen-ray and cathoderay generator used in this investigation. They also wish to acknowledge the able assistance of Augustus T. Norton, Jr. in this work.

#### REFERENCES

1. COOLIDGE, W. D., and MOORE, C. N. Some experiments with high voltage cathode rays outside of the generating tube. J. Franklin Inst., 1926, 202, 722-735.

2. Brasch, A., and Lange, F. Aussichten und Möglichkeiten einer Therapie mit schnellen Kathodenstrahlen. Strahlentherapie, 1934, 51,

3. TRUMP, J. G., and VAN DE GRAAFF, R. J. A compact pressure-insulated electrostatic x-ray generator. Phys. Rev., 1939, 55, 1160-1165.

4. Dresser, R., TRUMP, J., and VAN DE GRAAFF, R. J. Production of supervoltage roentgen rays by means of an electrostatic generator. Am. J. ROENTGENOL. & RAD. THERAPY, 1937, 38, 798-



# A COMPARATIVE ROENTGEN-RAY DIFFRACTION STUDY OF SEVERAL NATURAL APATITES AND THE APATITE-LIKE CONSTITUENT OF BONE AND TOOTH SUBSTANCE\*

By WILLIAM FREER BALE, Ph.D. ROCHESTER, NEW YORK

THE roentgen-ray diffraction evidence concerning the structure of the inorganic constituents of bone and tooth substance has consisted largely of the repeated observation that the powder diffraction patterns of these substances are similiar to that of fluorapatite. It had been suggested previously that bone and tooth substance was isomorphous with the mineral apatite from the results of chemical studies1 and from observations with polarized light.<sup>2</sup> Since tooth and bone substance contain little fluorine and considerable amounts of carbon it has been supposed by some that they are essentially carbonate apatites, with carbonate ions replacing the fluorine in the apatite structure.

Quantitative data concerning the variations in the structure of tooth and bone substance from that of fluorapatite are quite meager. Two independent determinations of the structure of apatite itself have been published. They are similar except that St. Náray-Szabó<sup>3</sup> places the fluorine ions at the  $oo_{\frac{1}{4}}$ ,  $oo_{\frac{3}{4}}$  positions of the unit cell, while Mehmel<sup>4</sup> gives their position as 000, 00½. Hendricks, Jefferson and Mosley<sup>5</sup> have measured the unit cell dimensions of bone and related substances. They state that florapatite, hydroxylapatite, oxyapatite, tricalcium phosphate hydrate and bone all have different diffraction patterns and can be thus identified. From packing considerations, they suggest a structure for bone as a carbonateapatite hydrate. Klement and Trömel<sup>6</sup> deny the existence of oxyapatite and tricalcium phosphate hydrate as crystalline entities, and state that the diffraction pattern of bone is the same

as hydroxylapatite and that therefore bone is essentially hydroxylapatite. Hodge, Le-Fevre and Bale,7 and Thewlis, Glock and Murray, among others, have also concluded that tooth and bone substance are essentially hydroxylapatites. Reynolds, Corrigan, Hayden, Macy and Hunscher<sup>9</sup>, state that the diffraction pattern of calcium fluoride appears along with that of hydroxylapatite in the teeth of rats fed excessive amounts of fluorine. Reynolds, Hayden and Corrigan<sup>10</sup> repeat that bone from a case of hyperthyroidism showed a diffraction pattern different from apatite. In all cases, with the exception of St. Náray-Szabó's apatite determination, intensity measurements have been limited to visual determinations from diffraction photographs. It is therefore difficult to judge between conflicting reports as to whether two substances do or do not give equivalent diffraction patterns. Due to this lack of quantitative experimental data, the only statement that can be made with certainty from roentgen-ray diffraction data is that tooth and bone substance is largely an apatite-ike material.

It seemed therefore worth while to measure quantitatively the diffraction spectra of these related substances in an effort to make the present knowledge concerning the structure of tooth and bone substance more precise. Long radius cassettes, a Bragg type ionization spectrometer suitable for either single crystal or powder spectra measurements, and a powder spectra measurements, and a powder spectrometer utilizing a Geiger-Müller counter as a suitable detector for weak diffraction maxima, were used in obtaining these data.

<sup>\*</sup> From the Division of Radiology, Department of Medicine, of the University of Rochester, School of Medicine and Dentistry and Strong Memorial Hospital, Rochester, New York.

EXPERIMENTAL DATA (PHOTOGRAPHIC)

A total of thirty-five natural apatites or minerals supposedly resembling apatite in structure has been studied by roentgen-ray diffraction methods.\* The roentgen-ray diffraction patterns of eighteen out of twenty minerals described as fluorapatites from widely distributed points of the world and in many cases of widely varying appearance are apparently identical. The diffraction patterns of two others of the fluorapatite samples were identical with these except that there were superimposed patterns of obvious mineral impurities. Collophanite from the island of Mona (described as monite) has a fluorapatite diffraction pattern. Other collophanites (described as pebble rock phosphate) have a diffraction pattern entirely dissimilar to that of apatite. Of special interest were several apatite-family minerals reported as containing considerable amounts of carbonate, and often described as calcium carbonate phosphates. Of these minerals, two specimens described as dahllite, and one specimen described as francolite gave distorted apatite-like diffraction patterns, considerably different from fluorapatite, however, both as to line positions and intensities. Three specimens of staffelite from different localities, one specimen of osteolite, and one specimen of koprolite gave diffraction patterns indistinguishable from fluorapatite.

Powdered bone substances, dentine, and enamel give diffraction patterns which, both as to line positions and intensity, are very similar to diffraction patterns of fluorapatite. Small, but definite and consistent differences do exist, however, as to line positions and comparative intensities. Tooth and bone substance, and fluorapatite are much more alike than either is to any of the other apatite-like diffraction patterns previously mentioned.

The preferential crystal orientation that is present in intact enamel, and which accounts for its distinctive diffraction

pattern, has been described adequately by Thewlis<sup>11</sup> and by Bale and Hodge<sup>12</sup> elseelsewhere. The diffraction pattern of powdered tooth enamel (in 17 separate samples and 200 different pictures) has always been that of an apatite-like substance with characteristics and constant deviations from fluorapatite. The diffraction pattern of powdered enamel is sharp and precise with a background of general scattering nearly as low as powdered apatite. The diffaction maxima, however, appear slightly broader than those of apatite taken under similar conditions of high resolution. There has never been any evidence of grain in the diffraction picture due to crystals of appreciable size in the enamel. Single approximately homogeneous crystals are therefore always very small. Size estimates have been published elsewhere.13

Dentine and the inorganic portion of bone substance give similar diffraction patterns distinguished by broader and more diffuse intensity maxima than is characteristic of enamel. Dentine, when untreated except for powdering, has a much greater background of generalized scattering than enamel. This background is appreciably decreased but still much greater than enamel when the organic material is extracted from dentine by the glycol ash method described by LeFevre, Bale and Hodge.<sup>14</sup> When starch is mixed with enamel in proportions to produce about the same amount of generalized scattering as is present in dentine, many of the fainter enamel lines are still distinguishable. These lines are not visible in dentine (or bone) even though the principal dentines may be more intense than the corresponding ones of enamel. Except for these differences ascribable to small crystal size, the diffraction patterns of dentine and bone substance are the same as those produced by tooth enamel. The same features are present in the diffraction pattern of bone and dentine that distinguish enamel from fluorapatite, and more noticeably from the other apatite-like natural minerals.

<sup>\*</sup> All natural minerals were obtained from Ward's Natural Science Establishment, Rochester, N. Y

In connection with a chemical study, diffraction patterns of a large number of primary, secondary, and tertiary calcium phosphates as well as hydroxylapatites were prepared. The detailed results of this work are reported elsewhere<sup>7</sup> and only those results will be described here that are directly pertinent to the structure of teeth and bone. The tricalcium phosphates examined gave in each case diffraction patterns that were either, so far as could be told by visual examination, the same as the diffraction pattern of tooth and bone substance or consisted of this diffraction pattern and superimposed upon it the diffraction pattern of one of the modifications of secondary calcium phosphate. The diffraction maxima of these tricalcium phosphates were more diffuse than the diffraction maxima of enamel. Hydroxylapatites have diffraction patterns also indistinguishable from those of dentine and bone, with the exception that the diffraction maxima were usually more sharp; often they were indistinguishable from tooth enamel. By contrast, certain of the tricalcium phosphates gave diffraction patterns so diffuse that they had almost the appearance of the diffraction patterns of liquid or amorphous substances.

On ignition at 900° C. the diffraction pattern of fluorapatite is unchanged. The effect of ignition on the higher calcium phosphates<sup>10</sup> depends upon both the calcium-phosphate ratio and the mode of preparation. On igniting samples with the theoretical chemical composition of tricalcium phosphate and precipitated by adding calcium ions to phosphate, a distinctive pattern called  $\beta$  tricalcium phosphate<sup>15</sup> is produced. Samples with the theoretical composition of hydroxyapatite, precipitated by adding phosphate to calcium, on ignition showed only the unignited pattern with a further sharpening of the diffraction maxima.

In enamel there was no very evident change on ignition. There is some sharpening and increase in intensity of the weaker diffraction maxima. On igniting dentine three different results have been obtained: (1) in most cases there has been only a sharpening of the diffraction maxima to an appearance similar to that of enamel; (2) certain specimens have undergone a partial change to the  $\beta$ Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> pattern; (3) in certain instances, there has been an increase in the c-dimension of the unit cell which results in a diffraction pattern resembling that of chlorapatite. This pattern has been duplicated by igniting Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> plus calcium chloride in amounts theoretical for chlorapatite.

A study of tooth sections using the pinhole diffraction method showed no change in the enamel pattern after ignition, either in the material present or in the preferential orientation of the crystalline constituent. Small change in the nature of the diffraction pattern would not have been detected by this method, due to the large and variable changes from the normal pattern caused by the preferential crystal orientation.

#### QUANTITATIVE INTENSITY DATA

The ionization spectrometer was used to study the powder diffraction spectra of enamel and fluorapatite quite extensively, and to make less elaborate measurements on the diffraction patterns of dentine, bone, ignited enamel and the various available hydroxylapatite and tricalcium phosphate samples. Mo  $K\alpha$  radiation filtered through zirconium oxide was used in every case. Three different methods of holding the diffracting sample could be utilized permitting (a) reflection from a surface, (b) transmission through a powder cake of uniform thickness with the incidence beam at the Bragg angle from the normal, and (c) transmission through a round thin-walled glass tube filled with the substance being examined. The data presented in Figures 1 and 2 were obtained by the third method. With the narrow slit system used, experiments showed that, with angles up to 20 degrees, this method closely approximated transmission through a slab of uniform thickness.

Figure 1, a, represents the diffraction pattern of fluorapatite as determined by the roentgen-ray spectrometer. The lower curve (Fig. 1, b) represents the same diffraction pattern with the background of general scattering removed as well as possi-

evident, as are also the variations, mainly quite small, of positions and of relative intensities of corresponding diffraction maxima.

It has been stated<sup>6,17</sup> that the diffraction pattern and therefore presumably the unit

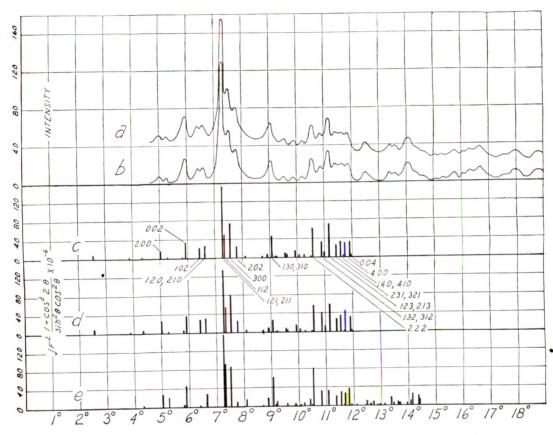


Fig. 1. Fluorapatite diffraction data, a represents the powder diffraction spectra of apatite as measured with the ionization spectrometer, plotted with ionization intensity as ordinate and  $\theta$  as abscissa, b is the same as a except that the background of general scattering has been removed graphically, e is the diffraction spectra calculated from the apatite structure proposed in this paper, d is the diffraction spectra calculated from St. Náray-Szabó's proposed apatite structure, e is the diffraction spectra predicted by St. Náray-Szabó's calculated F-values for apatite.

ble by graphical analysis. Figure 2, a and b, shows the corresponding data for tooth enamel. Other experiments utilizing the ionization spectrometer, the powder spectrometer equipped with Geiger-Müller counter, densitometric records, and visual inspection, show that both these records are acceptable as typical intensity measurements of the diffraction patterns. The great similarity in the diffraction spectra of the tooth enamel and fluorapatite is

cell of tooth and bone substance and of hydroxylapatite are identical, and that oxyapatite and tricalcium phosphate hydrate do not exist as crystalline entities. <sup>6,18</sup> Other investigators, <sup>5</sup> however, have stated that hydroxylapatite, tricalcium phosphate hydrate, oxyapatite and bone give sufficiently different diffraction patterns so that these substances may be recognized from their characteristic pattern. The latter reports have also given

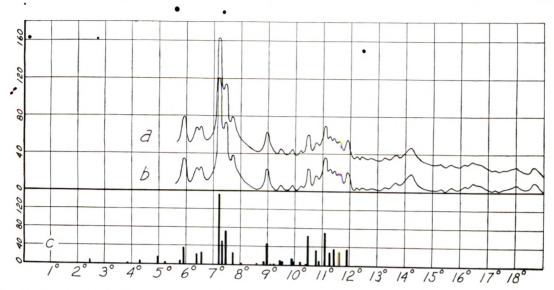


Fig. 2. Tooth enamel diffraction data. a represents the powder diffraction spectra of tooth enamel as measured with the ionization spectrometer, plotted with ionization intensity as ordinate and  $\theta$  as abscissa. b is the same as a except that the background of general scattering has been removed graphically. c represents the diffraction spectra of apatite as calculated from the fluorapatite structure proposed in this paper with the exception that the diffraction angles used are those of tooth enamel rather than of apatite.

measurements for these substances (recorded in Table 1) of unit cell dimensions which differ among themselves in some cases by several times the experimental error. Because of this conflicting evidence it seemed wise to measure these different units as accurately as possible.

The powdered substance being studied was held in a thin-walled, glass tube. For calibration and also to eliminate errors due to absorption or to variations in the physical set-up of the various experiments, a mixture of either NaCl or of SiO<sub>2</sub> and the substances being studied were used. The

criterion for designating a given sample as tricalcium phosphate hydrate was that on ignition at 900° C. it should be entirely transformed into  $\beta$  tricalcium phosphate. Similarly the criterion for hydroxylapatite was that the diffraction pattern should be heat stable at 900° C.

For the measurement of the a-dimension of the unit cell the 130 plane diffraction maxima were used, since it is well separated from confusing lines. For the c-dimension, measurements of 002 and 004 maxima were made. Figure 3 shows typical experimental data for each of these sub-

Table I
UNIT CELL DIMENSIONS OF SOME APATITE-LIKE SUBSTANCES

	Previously Reported Values		Present Values	
	a	С	a	С
Apatite	9 · 37 ± · 01	6.88 ± .01	9.37 ± .02	6.88 + .02
Bone	$9.27 \pm .03$	$6.95 \pm .03$	$9.48 \pm .04$	$6.88 \pm .04$
Tooth enamel Hydroxylapatite			9·47 ± .03	6.88 ± .03
Oxyapatite and ignited bone	9.40±.03 9.38±.03	$6.93 \pm .03$	$9.47 \pm .03$	$6.88 \pm .03$
Tricalcium phosphate hydrate	$9.30 \pm .03$ $9.25 \pm .03$	$6.93 \pm .03$ $6.88 \pm .03$	$9.47 \pm .03$ $9.47 \pm .05$	$6.88 \pm .03$ $6.88 \pm .05$

The previously reported values for apatite given above are those of St. Náray-Szabó. The values for the other substances are those given by Hendricks, Jefferson and Mosley. Thewlis, Glock and Murray have published values for apatite, tooth enamel, and hydrox-valuatite that within the reported experimental error are in agreement with the results of the present authors.

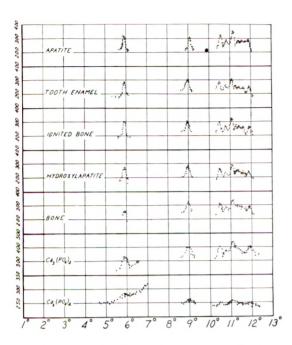


Fig. 3. Experimental powder diffraction data. The above data on apatite-like substances are plotted directly as recorded from a powder diffraction spectrometer utilizing a Geiger-Müller counter for intensity measurements. The ordinate is in terms of counts per minute, abscissa in terms of  $\theta$ . Each point represents the average counts per minute of a five minute run of the counter apparatus. The physical set-up of slit widths, dimensions of diffracting sample, etc, was the same for each of those five experiments.

The first  $Ca_3(PO_4)_2$  curve is typical of most commercial tricalcium phosphate. The last curve indicates the extreme imperfection of the crystal structure of certain preparations with the calcium-phosphorus ratio of tricalcium phosphate.

stances. Due to the good resolving powers of the apparatus the relative widths of the diffraction maxima of apatite, enamel and hydroxylapatite can be compared with those of heat labile Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>, dentine and bone. It is believed that these experiments demonstrate conclusively that within very close limits the unit cell dimensions of enamel, dentine, bone, tricalcium phosphate hydrate, hydroxylapatite and ignited bone are the same.

Using the ionization spectrometer, structure factor measurements were made on a good fluorapatite crystal on the oo2 to the oo8 planes and also on the 100 to the

700 planes. These values are recorded in Table III. It may be noted that they are in good agreement with the published values of St. Náray-Szabó. Absolute intensity measurements leading to absolute F-value determinations were also made on the 002 and 130, 310 powder diffraction maxima of fluorapatite and tooth enamel. These values are included in Table III.

# DISCUSSION OF EXPERIMENTAL FINDINGS

Roentgen-ray diffraction data on bone and teeth are confined entirely to powder measurements since single large crystals of these substances do not occur. Since fluorapatite can be obtained in large crystals and is thus more easily susceptible to roentgen-ray analysis, a logical approach to the problem of determining the structure of the bone and tooth unit cell is to determine what changes from the structure of fluorapatite are required for this substance to produce the diffraction pattern of bone and tooth substance. Also it should be possible to calculate whether any proposed structures for bone substance are inconsistent with this similarity of diffraction patterns.

It is necessary to know how closely the accepted structure of apatite will account for the experimental apatite diffraction pattern. Apatite belongs to space group C<sub>6h</sub><sup>2</sup>, the contents of the unit cell being Ca<sub>10</sub>F<sub>2</sub>(PO<sub>4</sub>)<sub>2</sub>. Determinations of its structure have been published by Mehmel<sup>4</sup> and by St. Náray-Szabó.3 Mehmel's structure determination, once the space group had been established, is based entirely upon packing and symmetry considerations. The structure given by St. Náray-Szabó is summarized in Table II. The roentgen-ray spectrometer was used by the latter to give absolute intensity measurements on the ooi, 110, and 100 crystal faces. Calculated structure factors were also correlated with visual intensity estimates from a powder photograph of apatite. He describes the agreement as good. Mehmel's proposed structure is similar to that of St. Náray-Szabó except that Mehmel placed the two fluorine ions at the  $000, 00\frac{1}{2}$  positions of the unit cell, rather than at the  $00\frac{1}{4}, 00\frac{3}{4}$  positions.

In the case of a few isolated diffraction maxima, it is possible to obtain experimental F-values directly from powder diffraction data to compare with the values calculated from St. Nàray-Szabó's proposed structure. I, the intensity of a powder diffraction maxima, may be measured as the increased area under the diffraction maxima as compared with the adjacent background on intensity-diffraction angle graphs. I is usually considered to have the value:

$$I = K \mathcal{I} \frac{\cos^2 2\theta}{\sin^2 \theta \cos^2 \theta} F^2.*$$

K is a constant that may be evaluated either experimentally or from a knowledge of the physical constants of the apparatus. To obtain the results reported here, NaCl or SiO<sub>2</sub>, substances with known structure factors, were mixed with the substance being studied to permit measurements of diffraction maxima in terms of the transmitted beam. In Table III are

TABLE II

THE STRUCTURE OF APATITE

Atomic positions

- I F (a)  $00\frac{1}{4}$ ,  $00\frac{3}{4}$ .
- 4 Ca<sub>I</sub> (f)  $\frac{1}{3}$ ,  $\frac{2}{3}$ , u;  $\frac{2}{3}$ ,  $\frac{1}{3}$ ,  $\bar{u}$ ,  $\frac{1}{3}$ ,  $\frac{2}{3}$ ,  $\frac{1}{2} u$ ;  $\frac{2}{3}$ ,  $\frac{1}{3}$ ,  $u + \frac{1}{2}$ .
- 6 Ca<sub>II</sub>, 6 P, 6 O<sub>I</sub>, 6 O<sub>II</sub>(h),  $uv_{4}^{1}$ ;  $u\bar{v}_{3}^{3}$ ;  $u\bar{v}_{4}$ ; u-v, u-v,
- 12 O<sub>III</sub> (i) xyz;  $\bar{x}\bar{y}\bar{z}$ ; x-y, x, z;  $\bar{y}$ , x-y, z; x, y,  $\frac{1}{2}-Z$ ;  $\bar{x}$ ,  $\bar{y}$ ,  $\frac{1}{2}+z$ ; x-y; x,  $\frac{1}{2}+z$ ;  $\bar{y}$ , x-y,  $\frac{1}{2}-z$ ; y, y-x,  $\frac{1}{2}+z$ ; y-x,  $\bar{x}$ , z; y, y-x,  $\bar{z}$ ; y-x, x,  $\frac{1}{2}-z$ .

Parameter Values, according to St. Náray-Szabó.3

	x/a	y/a	z/c
2 F	0	0	0.250
4 Ca <sub>I</sub>	0.333	0.333	0
6 Ca <sub>II</sub>	0.250	0	0.250
6 P	0.416	0.361	0.250
6 O <sub>I</sub>	0.333	0.500	0.250
$6 O_{III}$	0.600	0.467	0.250
12 O <sub>III</sub>	0.333	0.250	0.062

Suggested new 6 Ca<sub>II</sub> Parameters

6 Ca<sub>II</sub> 0.237 -0.015 0.250

listed experimental values for several diffraction maxima of apatite and tooth enamel.

In general, however, it is not possible to obtain individual F-values from the experimental powder diffraction spectra of apatite. This is because the powder diffraction maxima are often so close together that

Table III  $\begin{tabular}{ll} \textbf{EXPERIMENTAL DIFFRACTION DATA APATITE (MoK$\alpha=.710 Å)} \end{tabular}$ 

Indices	$\sin \theta$	F (exp) St. Náray-Szabó	F exp. (Bale) single crystal	F exp. powder	F exp.
002	0.1035	-135	I <b>1</b> 7	108	112
004	. 2070	188	202	100	112
006	.3105	85	70		
008	.4104	99	90		
100	.0436	0	15		
200	.0872	24	28		
300	. 1308	132	IIO		
400	.1744	18	18		
500	.2180	17	12		
600	. 2616	23	18		
700	. 3052	19	18		
130, 310	.1579			98	102

<sup>\*</sup> For the source and justification of this expression see Wyckoff, R. W. G.: "The Structure of Crystals." Second Edition (1931). The Chemical Catalogue Co., New York, or Bragg and West.<sup>19</sup>

they cannot be independently resolved and because planes with indices of the type ABC and BAC have different F-values but coincident diffraction maxima.

The method adopted for comparing calculated F-values with intensities of the experimental spectra in such cases was to calculate by the aid of expression the diffraction spectra predicted by these calculated F values, and to compare it with the experimental curve. Figure 1, e, represents graphically intensities I, which are calculated using St. Náray-Szabó's calculated F-values, and his values for the Bragg angle recalculated for Mo  $K\alpha$  radiation. This chart may be considered to be the powder diffraction pattern predicted by St. Náray-Szabó for apatite and therefore may be compared with the experimental curve 1, b. A similarity in the line intensities and positions of the experimental and constructed diffraction patterns is apparent. There may also be noted at various points quite wide variations between the two diagrams. The predicted diagram varies more widely from the experimental apatite curve than the experimental curve of tooth enamel does. Therefore the diagram constructed from St. Náray-Szabó's Fvalues cannot be of any great value in determining the difference in structure between tooth enamel and apatite.

As a first step toward a better understanding of the powder diagram of apatite, a recalculation of F-values from St. Náray-Szabó's apatite structure was undertaken. This was to detect, if possible, any errors that might be embodied in his F-values. It should be noted that errors that would be unimportant in his structure determinations become important in differential studies of substances with fundamentally similar structures. Experimental F-values as functions of  $\theta$  for  $O^{2-}$  and  $P^{6+}$  have been computed by West<sup>20</sup> from the results of his structural determination of KH<sub>2</sub>PO<sub>4</sub>. Experimental Ca2+ values are given by Bragg and West. 19 These are probably the values used by St. Náray-Szabó in his F calculations. The source of his F values

for fluorine is not known. F values for F-given by Wyckoff and Armstrong<sup>21</sup> have been used for the calculations reported here. All of these F values are in general quite similar to values given by other observers for these ions, which is perhaps an indication of at least an approximate correctness.

Structure factor values up to angles including the 004 diffraction maxima were calculated. The results are tabulated in Table IV. Figure I, d, represents calculated diffraction patterns computed from these values in the same manner as Figure I, e. It will be noted (Fig. I, d) that the agreement is considerably better between this calculated diffraction pattern and the experimental one than in the preceding case. This is evidence that the structure as determined by St. Náray-Szabó is essentially correct.

The agreement between predicted and experimental powder diffraction spectra is still not as good as it was hoped to obtain. Referring to Tables III and IV the calculated F-value for 130, i.e. +82.2, is considerably smaller than the experimental value of 98. The F-value of 310 is small and it would take considerable structural variation to make its contribution to this diffraction maxima of any significance. For 130 the oxygen contributions are calculated as 82 of a possible 96. This value cannot be greatly increased by a change in oxygen parameters. Shifts of the phosphorus parameters in various directions indicate that any likely P position cannot greatly increase the F-value of the cell. The F-value of fluorine is the same in either the ooo or oof positions, 11.8. Thus only a shift in the parameters of the 6 Ca ions appears likely to increase the F-value of the 310 maxima sufficiently. Tests show that a shift in these parameters from the .250,.000,.250 positions of St. Náray-Szabó to .237, -.015, .250 substantially improves the agreement between calculation and experiment. Other calculations show that there is an improved correspondence at other points in the diffraction pattern

Table~IV calculated diffraction data for apatite (Mo  $K\alpha$  = .710 Å)

_			Apatite			
Indices (Miller)	Apatite $\theta$	Tooth enamel $\theta$	F calc. by St. Náray- Szabó	F calc. from St. Náray- Szabó Structure	F calc. with new Ca positions	Number of planes
100	2° 33′	2° 28′	- I2	- 13	- II	6
101	3° 52′				5	12
110	4° 21′	3° 51′ 4° 18′	7	4	6	I 2
200	5° 1′	4° 58′	- 42	- 40	- 34	6
III	5° 16′	5° 14′	- 30	- I2	- 9	I 2
201	5° 49′	5° 47′	17	19	8	12
002	5° 55′	5° 55′	-124	-115	-109	2
102	6° 26′	6° 26′	- 12	- 43	- 38	12
120	6° 38′	6° 34′	- 23	- 18	- 14	6
210	6° 38′	6° 34'	- 57	- 63	- 60	6
121	7° 17′	7° 13′	- 62	- 62	- 57	12
211	7° 17′	7° 13′	- 92	- 82	- 93	12
112	7° 21′	7° 20′	87	66	70	12
300	7° 32′	7° 28′	I 2 I	118	112	6
202	7° 47′	7° 44′	- 30	- 48	- 44	12
301	8° 6′	8° 2′	39	24	15	12
220	8° 43′	8° 37′	- 20	7	• 2	6
122	8° 55′	8° 52′	32	6	9	12
212	8° 55′	8° 52′	- 32	- 30	- 18	12
130	9° 4′	8° 59′	118	74	95	6
310	9° 4′	8° 59′	- 2	- 18	- 35	6
221	9° 13′	9° 7′	- 22	- 7	- 18	12
103	9° 15′	9° 15′	- 28	4	7	12
131	9° 34′	9° 28′	24	23	19	12
311	9° 34′	9° 28′	0	- 24	- 26	12
302	9° 37′	9° 33′	28	24	34	12
113	9° 56′	9° 54′	25	44	41	12
400	10° 5′	9° 58′	- 32	43	40	6
203	10° 15′	10° 13′	30	19	28	12
401	10° 31′	10° 25′ 10° 29′	12	13	96	12
222	10° 34′ 10° 52′	10° 47′	108	91	- 60	12
132	10° 52′	10° 47′	- 43 - 52	- 54 - 60	- 38	12
312	10° 52′ 10° 59′	10° 47′ 10° 53′	- 52 - 64	- 62	- 47	6
230	10° 59′	10° 53′	04	- 8	- 15	6
320	11° 10′	11° 6′	42	53	50	12
123 213	11° 10′	11° 6′	60	82	88	12
231	11° 24′	11° 17′	45	52	41	12
321	II° 24′	11° 17′	38	43	48	12
140	11° 34'	11° 26′	71	77	83	6
410	11° 34′	11° 26′	75	79	66	6
303	11° 34′ 11° 42′	11° 39′	- 19	- 15	- 21	12
402	11 43	11° 39′	- 70	- 90	74	I 2
004	110 55'	11° 39′ 11° 55′	204	187	187	2
411	11 57	11 50	- 9	,	21	12
141	11° 57′	11° 50′	31		- 5	12

produced by this small parameter shift.

Further small shifts of Ca, P, and O parameters in various likely directions gave no appreciable improvement in the agreement of predicted and experimental diffraction diagrams. These shifts tested were by no means all of the possible ones, the tests being limited by the excessive amount of time required for such calculations.

A shift in the fluorine positions from the values of St. Náray-Szabó to the 000, 001 positions possible improves the correspondence of the 222, 132 and the 402 diffraction values, experimental and calculated, but produces a definitely poorer agreement in the case of the 102, 200, and 112 planes. Most of the other intensity maxima are not affected by this shift. It is likely that there is a greater heat motion in the Z-direction for fluorine than has been assumed in the F-values assigned to fluorine for the previous calculations. As a possible corrective for this greater heat motion, it was assumed that the Z-parameters are thus indeterminate and 000,  $00\frac{1}{2}$ positions were given one-third the weight of the  $00\frac{1}{4}$ ,  $00\frac{3}{4}$  positions in structure factor calculations. Table IV gives the new Fvalues calculated assuming the new Ca positions and with the F-values for fluorine as described above. The calculated diffraction diagram shown in Figure 1, c, is obtained.\* The agreement between calculated value and experiment can be described as good. No serious disagreement is produced between St. Náray-Szabó's experimental F-values and F-values calculated on this assumption of this shift of the Ca parameters of the indeterminacy in the position of fluorine.

In Figure 2, c, has been plotted the calculated diffraction spectrum of apatite, using the data from which Figure 1, c, was

plotted with the exception that the  $\theta$ 's calculated from the experimentally measured unit cell of enamel and listed in Table IV have been utilized. It may be noted that the agreement between this curve and the experimental diffraction pattern for enamel directly above is good, in fact much better than the agreement between the experimental curve for enamel and the calculated apatite curve (Fig. 1, c). Therefore, the principal cause of the differences between the diffraction pattern of apatite and that of enamel, at least to diffraction angles as great as that corresponding to the 004 diffraction maxima, is the small but definite variation in unit cell dimensions.

Since the diffraction pattern of hydroxylapatite appears indistinguishable from tooth enamel, its structure must also be very close to that of fluorapatite. Probably the essential difference is the substitution for fluorine ions of the similarly sized hydroxyl ions.

Trömel and Möller,22 and Hodge, Le-Fevre, and Bale<sup>7</sup> have presented evidence from chemical studies that the so-called tricalcium phosphate hydrates are essentially hydroxylapatites with additional phosphorus present in what has been described as an absorbed state on the small hydroxylapatite crystals. The roentgen-ray diffraction measurements reported in this paper show increased width of the diffraction maxima of tricalcium phosphate as compared with hydroxylapatite but the same unit cell dimensions. This result, which is interpreted as indicating either the extremely small size of the crystals making up the tricalcium phosphate hydrate, or the great imperfection of these crystals, or both, is consistent with the interpretation given above based on chemical data.

Considerable amounts of carbon exist in bone and tooth substance, approximately sufficient to allow one CO<sub>3</sub><sup>2-</sup> per unit cell, although carbon is the most variable of the major constituents of teeth and bone. Since carbonates have never been identi-

<sup>\*</sup> In a private communication, Bredig has called attention to the difference in the number of theoretical and experimental maxima in Figure 1, especially in the region between diffraction angles 11 and 12 degrees. He suggests that such variations might arise from various proportions of CO<sub>3</sub> to F in a mixed apatite. It seems more likely, however, that this variation is due to random fluctuations in the experimental data, i.e., experimental errors, since other measurements show the theoretical number of maxima in this region.

fied in diffraction patterns of these substances as separate crystalline constituents, it is tempting to suppose that the carbonate forms an integral part of the crystal lattice of tooth and bone, and that these substances are therefore basically carbonateanatites. There are two possible positions for the carbonate radical in the apatite structure. Hendricks, Hill, Jacobs and Jefferson<sup>23</sup> suggest that the CO<sub>3</sub><sup>2-</sup> radical occupies the position of one of the F- ions of the unit cell, the empty position of the other fluorine ion being occupied by an uncharged water molecule. Hendricks, Iefferson and Mosley<sup>5</sup> later suggested that the water molecule and the carbonate radical are in the 000, and  $00\frac{1}{2}$  positions. Since the diffraction patterns of tooth and bone substance and of hydroxylapatite are so very similar it seems pertinent to inquire how much distortion of the apatite lattice would be produced by such substitutions. Several investigators have stated that there is not room in the apatite lattice for the carbonate radical. However, no quantitative data on this question have so far been published.

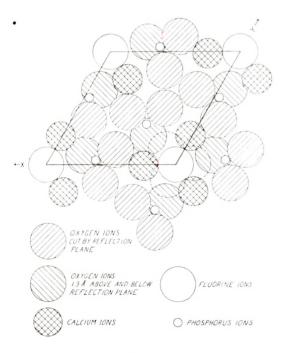


Fig. 4

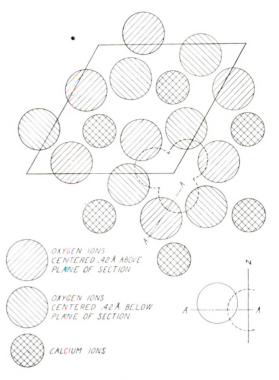


Fig. 5 .

Numerous investigators have studied the nature of the CO<sub>3</sub><sup>2-</sup> radical in several compounds, calcite perhaps most elaborately. In such compounds, without exception, the carbonate radical has been found to be strictly planar with the central carbon 1.26 Å from the centers of the surrounding O<sup>2-</sup> ions which are placed at the corners of an equilateral triangle 2.18 Å on a side. Between metallic ions (for instance, the calcium ions of calcite) and oxygen centers, the distance is that indicated by the usual O<sup>2-</sup> radius of 1.26 Å.

Figure 4 represents a section of the fluorapatite structure at the  $z=\frac{1}{4}$  level. The dotted figure indicates the space that the carbonate radical would occupy if it replaced fluorine at  $00\frac{1}{4}$ . Figure 5 is a section of the apatite structure at the z=0 level with the carbonate radical indicated in the 000 position. Even with considerable allowance for the slightly increased size of the hydroxylapatite lattice and for variations in packing size it seems quite unlikely that a carbonate apatite would be

formed without marked variation in atomic parameters as compared with a hydroxylapatite containing no carbonate. Calculations show that even small variations in atomic parameters should produce noticeable variations in the diffraction pattern. It is therefore unlikely that the diffraction pattern of bone substance is principally that of a carbonate apatite, although occasional replacements of this type may exist.

Gruner, McConnell and Armstrong<sup>24</sup> suggest that carbon may replace calcium and also phosphorus in the apatite structure of bone and tooth substance, giving in the case of phosphorus replacement a CO<sub>4</sub> grouping. The data presented here can neither affirm nor deny these hypotheses. However, this structure seems unlikely since carbon is not known otherwise to form this type of structure.

It is probable that the portion of tooth and bone substance responsible for its characteristic diffraction pattern is essentially hydroxylapatite. That variations and distortions of this apatite structure are common in tooth and bone substance is indicated by the increased breadth of the diffraction maxima of these substances as compared with fluorapatite. It is in such structural discontinuities that the excess phosphate of tricalcium phosphate hydrate is probably found. Since the diffraction patterns of tooth and bone substance give no indication of appreciable amounts of a carbonate apatite being present, the carbonate ions are also, probably, most abundant in these regions of structural discontinuity that may be considered as marking the transition from one crystalline particle to another. Thus the carbonate contribution is mainly to the random element responsible for the diffuseness of the hydroxylapatite diffraction pattern of tooth and bone rather than toward producing a characteristic carbonate apatite diffraction spectrum of its own.

I wish to thank Dr. Stafford L. Warren, Dr. Harold C. Hodge, Miss Marian LeFevre, and Mr. Francis Bishop for assistance in various phases of this work. This work was supported in part by a grant from the Rockefeller Foundation.

#### SUMMARY AND CONCLUSIONS

- 1. Powder diffraction data reported here indicate that the structure proposed by St. Náray-Szabó for fluorapatite must be nearly correct. Slight shifts in the apatite parameters are found, which give appreciably better agreement between calculated diffraction intensities and the diffraction data reported. Parameters of these structures are given in Table II.
- 2. The dimensions of the unit cells of bone, tooth enamel, dentine, hydroxylapatite and tricalcium phosphate hydrate are measured and are found to be identical within the range of experimental error. They give closely similar apatite-like patterns which, in minor points mainly due to a difference in the a-dimension of the unit cell, are significantly different from fluorapatite.
- 3. That portion of bone and tooth substance responsible for its characteristic diffraction pattern tends to approximate the structure of hydroxylapatite. It is concluded, however, that present roentgenray diffraction evidence is consistent with a considerable lack of homogeneity in the nature of tooth and bone substance.
- 4. Probably the carbonate present in tooth and bone substance does not form an integral part of the apatite lattice, but is rather present, for the most part at least, at boundary and transition regions in the lattice where the apatite structure is imperfectly developed.

#### REFERENCES

- I. Bassett, H. The phosphates of calcium, Part IV. J. Chem. Soc., 1917, 3, 620-642.
- 2. Schmidt, W. I. Ueber die Orientierung der Kristallite in Zahnschmelz. Sitzeber. naturwiss. Abt. Niederrh. Ger. T. Natur. u. Heilk., 1923, 1-19 (Bonn, 1925).
- 3. St. Náray-Szabó. The structure of apatite. Z. Krist., 1930, 75, 387-398.
- 4. Mehmel, M. Ueber die Struktur des Apatits. Z. Krist, 1932, 81, 323-331.
- 5. Hendricks, S. B., Jefferson, M. E., and Mos-Ley, V. M. The crystal structures of some nat. ural and synthetic apatite-like substances. Z-Krist., 1932, 81, 352-369.

- KLEMENT, R., and TRÖMEL, G. Hydroxylapatit,
   der Hauptbestandteil der anorganischen Knochen- und Zahnsubstanz. Ztschr. f. physiol. Chem., 1932, 213, 263-269.
- 7. Hodge, H. C., LeFevre, M. L., and Bale, W. F. Chemical and x-ray diffraction studies of calcium phosphates. *Indust. & Engin. Chem.*, 1938, 10, 156-161.
- THEWLIS, J., GLOCK, G. E., and MURRAY, M. M. Chemical and x-ray analysis of dental, mineral, and synthetic apatites. *Tr. Faraday* Soc., 1939, 35, 358–363.
- 9. REYNOLDS, L., CORRIGAN, K. E., HAYDEN, H. S., MACY, I. G., and HUNSCHER, H. A. Diffraction studies of the effect of sodium fluoride and parathormone upon the incisors and tibiae of rats. Am. J. ROENTGENOL. & RAD. THERAPY, 1938, 39, 103–126.
- IO. REYNOLDS, L., HAYDEN, H. S., and CORRIGAN, K. E. Diffraction studies on human bone. Am. J. ROENTGENOL. & RAD. THERAPY, 1938, 39, 286–287.
- II. Thewlis, J. X-ray analysis of teeth. Brit. J. Radiol., 1932, 5, 353-359.
- 12. BALE, W. F., and Hodge, H. C. Ueber die Kristallorientierung im Zahnschmelz. *Naturwissenschaften*, 1936, 24, 141–142.
- 13. BALE, W. F., HODGE, H. C., and WARREN, S. L. Roentgen-ray diffraction studies of enamel and dentine. Am. J. ROENTGENOL. & RAD. THERAPY, 1934, 32, 369–376.
- 14. LeFevre, M. L., Bale, W. F., and Hodge, H. C. The chemical nature of the inorganic portion of fetal tooth substance. J. Dent. Research, 1937, 16, 85–101.
- 15. TRÖMEL, G. Beiträge zur Kenntnis des Systems Kalziumoxyd-Phosphorpentoxyd. *Mitt. Kaiser-Wilh. Inst. Eisenforsch.*, 1932, 14, 25–37.

- 16. Bale, W. F., Hodge, H. C., and LeFevre, M. L. Ueber der anorganischen Aufbau der Zähne. Naturw seenschaften, 1936, 24, 636.
- 17. Bredig, M. A. Zur Apatitstruktur der anorganischen Knochen- und Zahnsubstanz. Zischr. f. physiol. Chem., 1933, 216, 239-243.
- 18. Trömel, G. Untersuchungen über die Bildung eines halogenfreien Apatits aus basischen Kalziumphosphaten. *Phosphorsäure*, 1932, 2, 116-124.
- Bragg, W. F., and West, J. A technique for the x-ray examination of crystal structures with many parameters. Z. Krist., 1929, 69, 118– 148.
- 20. West, J. A quantitative x-ray diffraction analysis of structure of potassium dihydrogen phosphate. Z. Krist., 1930, 74, 306–332.
- 21. WYCKOFF, R. W. G., and Armstrong, A. H. The scattering powers of the atoms in magnesium oxide and sodium fluoride. Z. Krist., 1930, 72, 433-441.
- 22. TRÖMEL, G., and MÖLLER, H. Die Bildung schwer löslicher Calciumphosphate aus wässriger Lösung und die Beziehungen dieser Phosphate zur Apatitgruppe. Z. Anorgan u. allg. Chem., 1932, 206, 227–240.
- 23. HENDRICKS, S. B., HILL, W. L., JACOBS, K. D., and JEFFERSON, M. E., Structural characteristics of apatite-like substances and composition of phosphate rock and bone as determined from microscopical and x-ray diffraction examinations. *Indust. & Engin. Chem.*, 1931, 23, 1413–1418.
- 24. Gruner, J. W., McConnell, D., and Armstrong, W. D. The relationship between the crystal structure and chemical composition of enamel and dentine. J. Biol. Chem., 1937, 121, 771-781.



# THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Delegates to the Sixth International Congress of Radiology: Albert Soiland, Los Angeles, Calif., Delegate, Zoe A. Johnston, Pittsburgh, Pa., Alternate Delegate.

Twenty-fifth Annual Meeting: Hotel Waldorf Astoria, New York City, June 10-11, 1940.

### EDITORI AL

# INTRACRANIAL COLLECTIONS OF IODIZED OIL FOLLOWING LUMBER MYELOGRAPHY

ANDY, in 1919, was the first to use air in the spinal canal as a contrast medium for the localization of spinal cord lesions. Following quickly upon the heels of Dandy's observation, Sicard and Forestier introduced lipiodol into the spinal canal and this contrast medium has been of valuable aid in the diagnosis and localization of certain lesions of the spinal cord. This, however, has one disadvantage in that it has been known for a long time that the opaque oil remains indefinitely in the spinal canal unless it is removed at operation, which is usually very difficult and seldom can be accomplished as the oil often is scattered throughout the cerebrospinal fluid pathway. It has been believed for some time that the oil is somewhat irritating and that it may be encapsulated in or about the lower portions of the spinal sac. For this reason warnings have been issued against the indiscriminate use of opaque oil within the spinal canal.

Chamberlain and his coworkers have shown that with modern technique air may be useful as a contrast medium; particularly is this true in thin subjects, and Chamberlain has been the great exponent in advocating the use of air instead of opaque oils. However, in the hands of most observers the oil has furnished far more conclusive results than have the air myelographic studies.

Quite recently Garland and Morrissey\* became interested in the question of intracranial collections of iodized oil following myelography. A survey of the literature revealed no specific information on clinical symptoms or pathologic changes due to prolonged metention of lipiodol intracranially, although there was considerable material on late changes in and about the meninges of the cord. In order to throw a little more light on the problem and to study it under clinical conditions, they decided to have return for examination a group of patients who had had lipiodol injected into their spinal canal several years previously, and they have quite recently reported their observations.

It has been known for some time that there are certain reactions to the subarachnoid injections of iodized oil and also that mild reactions follow the injection of air. These reactions may be immediate as shown in the elevation of the spinal fluid cell count and slight hyperemia about the site of injection, and clinically there may be slight headache, increase in the pain of which the patient is complaining, slight fever, and sometimes pain about the sacrum and coccyx. These symptoms and clinical signs usually subside in from two to five days. Occasionally late reactions are manifested in coccygeal pain which usually subsides within three months. The oil may lie in small droplets and lakes scattered up and down the spinal canal, sometimes extending out along the nerve sheaths. Occasionally the oil may be encapsulated in the cul-de-sac at the base of the spinal canal. After about three years these droplets tend to become encapsulated in various areas and fibroblastic proliferation and pseudogranulomas may develop about the oil.

It is these late manifestations which have prompted neurosurgeons to attempt to remove some if not all of the oil at the time of laminectomy, but this is a rather

<sup>\*</sup> Garland, L. H., and Morrissey, E. J. Intracranial collections of iodized oil following lumbar myelography. Surg., Gynec. & Obst., Feb. 1, 1940, 70, 196-210.

difficult procedure and is not always accomplished, and it has been suggested by some that undue efforts at removal of the oil may do more harm than leaving the oil in situ.

Garland and Morrissey, in a review of their cases showing lipiodol in the cranial cavity, have attempted to clear up some of the clinical impressions regarding the presence of lipiodol or other opaque oil in the cranial cavity, since the previous reports on this have been somewhat vague.

The patients which they restudied had had subarachnoid lipiodol injections from one to thirteen years previously, 3 to 5 cc. of the oil having been used in most instances.

In the study their attention was called to the fact that iodized oil may be found scattered throughout the subarachnoid space over the cerebrum and cerebellum, in the basal cisternae, and even in the ventricles years after its injection into the lumbosacral sac. Approximately two-thirds of their cases showed collections of varying amounts of lipiodol intracranially but none of these patients except one exhibited any symptoms which were not present before the lipiodol injection was made. The one case that was somewhat at variance with these observations was a patient who proved later to be a malingerer. Garland

and Morrissey call attention to the danger of drawing premature conclusions from the finding of iodized oil in the leptomeninges of the brain and spinal cord. In their group of cases it was noted that the intracranial lipiodol tends to become fixed, that is, immovable, whereas iodized oil in the spinal canal, especially when in large collections, is sometimes freely movable even up to a period of fourteen years following injection. They were unable to explain why in only two-thirds of their cases iodized oil was found intracranially following the intraspinal injection. In order to determine this point they are inquiring into the patients' occupation or postural habits, whether the group that showed intracranial lipiodol were employed in work which involved frequent lowering of the head.

From a critical analysis of their cases they came to the conclusion that there were no symptoms or positive neurological findings which could be ascribed to the presence of the oil intracranially.

While it is of the greatest importance to learn that the presence of lipiodol in the intracranial cavity is not in itself productive of symptoms, the *indiscriminate* use of lipiodol in the study of suspected spinal cord lesions is to be deplored, and only in those carefully selected cases is one justified in using it as a diagnostic procedure.



#### SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the everts to which they refer.

#### MEETINGS OF ROENTGEN SOCIETIES\*

United States of America

AMERICAN ROENTGEN RAY SOCIETY

Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Hotel Statler, Boston, Mass., Oct. 1–4, 1940.

AMERICAN COLLEGE OF RADIOLOGY

Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Next Annual Meeting: Commodore Hotel, New

York City, June 12, 1940.
Section on Radiology, American Medical Association Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: New York City, June 10–14, 1940.

RADIOLOGICAL SOCIETY OF NORTH AMERICA

Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Cleveland, Ohio, Dec. 2-6,

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.
RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY

Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September.

Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each

month at County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY

Secretary, Dr. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY

Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to May inclusive at the Hotel Sherman.

CINCINNATI RADIOLOGICAL SOCIETY

Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY

Secretary, Dr. H. A. Mahrer, 10515 Carnegie Ave. Meets at 6:30 P.M. at Mid-Day Club rooms on fourth Monday each month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB

Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY

Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY

Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

ILLINOIS RADIOLOGICAL SOCIETY

Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meetings held quarterly, on the fourth Sunday of the month.

Indiana Roentgen Society

Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis,

Ind. Meeting held the second Sunday in May annually. KENTUCKY RADIOLOGICAL SOCIETY

Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville. Meets annually in Louisville on third Sunday afternoon

LONG ISLAND RADIOLOGICAL SOCIETY

Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGIST

Secretary, Dr. J. E. Lofstrom, 1536 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring. MILWAUKEE ROENTGEN RAY SOCIETY

Secretary, Dt. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis Meets monthly on first Friday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY

Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

Nebraska Ramological Society

Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

Secretary, D. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY

Secretary, Dr. W. J. Marquis, 198 Clinton Ave., Newark. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

NEW YORK REENTGEN SOCIETY

Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. T. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society.

Mid-year scientific meeting at place designated. CENTRAL NEW YORK ROENTGEN RAY SOCIETY

Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November. Pacific Roen Gen Club

Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY

Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Next annual meeting, Hershey Hotel, Hershey, Pa., May 17-18 1940.

PHILADELPHIA ROENTGEN RAY SOCIETY

Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY

Secretary, Dr. H. W. Jacox, 4800 Friendship Ave., Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y. Secretary, Dr. S. C. Davidson, 277 Alexander St. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

St. Louis Society of Radiologists
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY

Secretary, Dr. H. A. Hill: 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six mouths at Toland Hall, second six months at Lane Hall.

<sup>\*</sup> Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

SOUTH CAROLINA X-RAY SOCIETY Secretary, Dr. Hillyer Rudisill, Jr., Roper Hospital, Charleston. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY

Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society

Secretary, Dr. L. W. Baird, Scott and White Hospital,
Temple, Texas. Next annual meeting, January 18, 1941, Sherman, Texas.

University of Michigan Department of Roentgen-OLOGY STAYF MEETING

Meets each Monday evening from September to June,

at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00-5:00 P.M., Room 301, Service Memorial Institute. VIRGINIA RADIOLOGICAL SOCIETY

Secretary, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday of each month at the College Club, Seattle.

Sociedad Cubana de Radiologia y Fisioterapia Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

#### BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY

Meets monthly on third Thursday, from November to June inclusive, at 8:15 p.m., 32 Welbeck St., London. Section of Radiology of the Royal Society of Medi-

CINE (CONFINED TO MEDICAL MEMBERS)

Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1. FACULTY OF RADIOLOGISTS

Secretary, Dr. Barbara M. Key, 32 Welbeck St., London, W. 1, England.
Section of Radiology and Medical Electricity, Australasian Medical Congress

Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

RADIOLOGICAL SECTION OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION

Secretary, Dr. Keith Hallam, St. George's Hospital, K.F.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive for scientific discussion.

CANADIAN ASSOCIATION OF RADIOLOGISTS
Secretary, Dr. A. C. Singleton, Medical Arts Bldg.,

Toronto, 5, Ontario.
Section of Radiology, Canadian Medical Association Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S. RADIOLOGICAL SECTION, NEW ZEALAND BRITISH MEDICAL

Association Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

#### CONTINENTAL EUROPE

Belgian Society of Roentgenology Secretary, Dr. J. Boine, Avenue des Alliés; 134, Louvain (Belgium). Meets monthly on second Sunday at d'Eg-

monds Palace, Brussels, except in the summertime.
Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid,
Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris. Société Suisse de Radiologie (Schweizerische Rönt-GEN-GESELLSCHAFT)

Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale

Meets monthly on fourth Tuesday, except during months

of August and September, 12 Rue de Seine, Paris.
ASSOCIATION OF GERMAN ROBINTGENOLOGISTS AND RADIOLOGISTS IN CZECHO-SLOVAKIA Secretary, Dr. Walter Altschul, German University,

Prague, 11.52. Deutsche Röntgen-Gesellschaft (Gesellschaft für

RÖNTGENKUNDE UND STRAHLENFORSCHUNG) Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.

Permanent Secretary, Professor Dr. Hnenisch, Klopstock-

strasse 10, Hamburg, Germany. Süd- und Westdeutsche Röntgengesellschaft Meets annually in different cities.

NORD- UND OSTCEUTSCHE RÖNTGENGESELLSCHAFT

Meets annually in different cities. DUTCH SOCIETY OF ELECTROLOGY AND ROENTGENOLOGY

Holds two meetings a year in Amsterdam, one in the spring, and one in the fall.

Societa Italiana Radiologia Medica

Secretary, M. Ponzio, University of Turin, Prof. Turin Societatea Romana de Radiologie si Electrologie Secretary, Dr. Cscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in

every month with the exception of July and August.
ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.

Meets annually.

LENINGRAD ROENTGEN RAY SOCIETY

Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentoga Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly on first Monday at 8

Polish Society of Radiology Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

WARSAW SECTION, POLISH SOCIETY OF RADIOLOGY Secretary, Dr. B. Krynski, 11 Zielna St. Meets once a month except in the summertime.

SCANDINAVIAN ROENTGEN SOCIETIES

The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the fol-lowing societies, with exception of the Denmark Society, meets every second month except in the summertime:

SOCIETY OF MEDICAL RADIOLOGY IN SWEDEN Meets in Stockho.m.

SOCIETY OF MEDICAL RADIOLOGY IN NORWAY Meets in Oslo.

SOCIETY OF MEDICAL RADIOLOGY IN DENMARK Secretary, Dr. G. Biering, Copenhagen. Meets the second Wednesday of each month from October to July in Copenhagen, at & oclock in the State Institute of Roentgenology.

SOCIETY OF MEDICAL RADIOLOGY IN FINLAND Meets in Helsingfors.

Vienna Roentgen Society Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

#### ORIENT

JAPAN X-RAY ASSOCIATION c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April. KINKI ROENTGEN-ABEND SOCIETY

## AMERICAN ROENTGEN RAY SOCIETY

#### SECTION ON INSTRUCTION

B. R. KIRKLIN, M.D., Director

Abstracts of Courses Offered

Forty-first Annual Meeting

Hotel Statler, Boston, Massachusetts

October 1–4, 1940

President-elect Sosman, with the approval of the Executive Council, has directed that the Section on Instruction be continued for the 1940 annual meeting. He has arranged his program so that the instruction courses will be given between the hours of 2:00 P.M. and 4:30 P.M. on Tuesday and Thursday, and 2:00 P.M. and 5:45 P.M. on Wednesday and Friday. Nothing else will be scheduled during these hours, thus allowing everyone at the meeting to attend two or three instruction courses each afternoon.

This Section presents for 1940:

- 1. Four single-period Special Clinical Lectures.
  - 2. One three-period Sequential Course.
- 3. Two single-period courses on Miscellaneous Subjects.
- 4. Thirty-six single-period courses on Diagnostic Roentgenology, with a faculty of forty instructors and covering forty-two periods.
- 5. Twenty-five single-period courses on Therapeutic Radiology, with a faculty of twenty-six instructors and covering thirty-one periods.

#### GENERAL INFORMATION

#### Conference Periods

Tuesday, Wednesday, Thursday and Friday afternoons

First period. 2:00 to 2:50 Second period. 3:00 to 4:15
Wednesday and Friday afternoons
Third period 4:30 to 5:45

#### Location

One of the single-period Special Lectures, lettered "SL-I" to "SL-4" will be given during the first period (2:00 to 2:50 P.M.) each day. Due to the anticipated popularity of these Special Lectures no other courses will be scheduled for the first period on any day and they will be given in the Georgian Room on the Mezzanine Floor. All other courses given during the second and third periods will be given on the fourth floor.

The instruction periods will be designated with the following code:

T-1Tuesday, first period2:00 to 2:50
T-2Tuesday, second period3:00 to 4:15
W-1. Wednesday, first period 2:00 to 2:50
W-2 Wednesday, second period . 3:00 to 4:15
W-3Wednesday, third period4:30 to 5:45
Th-I. Thursday, first period 2:00 to 2:50
Th-2 Thursday, second period3:00 to 4:15
F-1Friday, first period2:00 to 2:50
F-2Friday, second period3:00 to 4:15
F-3Friday, third period4:30 to 5:45
7, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1,

(Familiarity with this code will avoid much confusion)

#### How to Secure Tickets for Instruction Courses

Admission to the Instruction Courses will be by ticket only.

Following the abstracts of the courses will be found a pink general order sheet. First, second and third choices for the second and third periods should be carefully selected as the number attending each course given during these periods will be limited to from thirty to fifty persons. It is not necessary to indicate second and third choices for the first period as only

one of the Special Clinical Lectures will be given during the first period each day. If directions as given on the order sheet are followed explicitly, errors in completing reservations will be minimized.

It is possible for one to attend only ten periods of instruction so the condensed schedule should be noted carefully in arranging individual orders for tickets.

Reservations will be made in the order of receipt of the pink forms. Those who are not members of the American Roentgen Ray Society will be charged a nominal fee of \$1.00 per period, or a maximum fee of \$5.00 for five or more periods. Full time graduate students in Radiology will be admitted without fee.

If the courses are not filled by the time of the meeting, tickets will be available at the registration desk, located on the Mezzanine Floor, on Sunday, September 29, and thereafter during the meeting.

#### Holders of Tickets

Those who do not have a proper ticket for the assigned course will not be permitted to enter the room. Pages will be assigned to each conference room to collect tickets.

#### Duplications and Repeats

Due to the anticipated heavy registration a few courses will be repeated and others will be duplicated by two or more instructors.

#### SPECIAL CLINICAL LECTURES

COURSE: SL-1

Georgian Room

Period: T-1

SHIELDS WARREN, M.D., Boston, Mass.

#### The Radiosensitivity of Tumors

The varied response of different types of tumors to radiation still rests on an empirical basis, although in general the less differentiated tumors respond better than highly differentiated ones. The response hinges not only on the character of the tumor itself, but also on the character of the supporting tissue, the pres-

ence or absence of associated infection, and whether or not previous radiation has been given.

Tumors may be grouped into three classes: radiosensitive, which regress with dosages that do no permanent damage to adjacent normal tissue; radioresponsive, that regress with doses producing moderate damage to normal tissue; and radioresistant, that fail to regress or do so only with dosages that do serious injury to normal tissues.

In the response to radiation, the direct effect on the type cell of the tumor, the alteration of the connective tissue of the stroma, and the injury to stromal blood vessels all play important parts.

The factors that bring about increased radioresistance of tumors following their initial irradiation are not clearly defined, but undoubtedly stromal and vascular changes play an important part.

Examples of various types of sensitive and resistant tumors will be shown.

#### COURSE: SL-2

Georgian Room

Period: W-1

#### GERRY B. SCHNELLE, V.M.D., Boston, Mass.

#### Roentgen Rays in Veterinary Medicine

This will be an "Information Please" type of program with the lecturer presenting roentgenograms of animals, showing the unusually varied diseases and tumors that animals are subject to. Most of these conditions can be readily diagnosed by their similarity to the roentgen findings in man.

There will be three "experts" who will take turns in attempting to make the diagnosis from the roentgenogram.

Lantern slides will be used for the audience.

#### COURSE: SL-3

Georgian Room

Period: Th-1

W. B. CASTLE, M.D., Boston, Mass.

#### Leukemia

A comprehensive clinical discussion of leukemia will be presented including the differential diagnosis, prognosis, treatment and care of patients from the non-radiological aspect.

#### COURSE: SL-4

Georgian Room

Period: F-1

FULLER ALBRIGHT, M.D., Boston, Mass.

#### Osteoporosis

The term "osteoporosis" will first be defined. In order to do this a schematic chart will be presented

which will represent the calcium and phosphorus metabolism in the normal individual. Schematic charts will then be presented of various generalized metabolic disorders. These will include osteomalacia, osteitis fibrosa, Paget's disease, and osteoporosis. The clinical conditions which lead to osteoporosis will then be discussed. One special entity which is termed post-menopausal osteoporosis will be emphasized. Some metabolic data showing the effects of hormonal therapy on post-menopausal osteoporosis will be presented. Certain cases will be discussed in which two metabolic bone diseases occurred in the same patient, e.g. osteoporosis and Paget's disease, osteoporosis and hyperparathyroidism.

#### SEQUENTIAL COURSE: A

Room: 400 Periods: T-2; W-2; Th-2

#### JOHN T. MURPHY, M.D., Toledo, Ohio Malignant Bone Tumors

Both the roentgenologic and microscopic findings of malignant tumors of bone will be shown and discussed. The clinical course of the disease will be stressed and a complete follow-up of each patient will be presented. Considerable time will be devoted to the differential roentgenologic diagnosis.

This course will be conducted as a teaching seminar and all those in attendance may participate in the discussion.

This is a sequential course and no part of it will be repeated.

#### SINGLE PERIOD COURSES

#### MISCELLANEOUS

COURSE: 101

Room: 412

Period: Th-2

ARIAL W. GEORGE, M.D., Boston, Mass.

#### Roentgenology in Industrial Medicine and Automobile Accidents; The Roentgenologist as an Expert Witness

This course will consist of a discussion of:

- I. The importance of careful and concise reports on industrial and accident cases.
- The importance of exactness of diagnosis and proper use of medico-roentgenologic terms (nomenclature).
- 3. The rôle that industrial and accident roentgenology plays in medicolegal expert testimony.
- 4. Some of the pitfalls that experts, especially roentgenologists, are likely to encounter.
- 5. Some of the fundamentals of court procedure

- relative to the plaintiff as well as the medicolegal expert (roentgenologist) for the defense the latter's rights under the law.
- The controversial subject "Arthritis of the Vertebrae" and its importance in industrial roentgenology.

The instructor will be glad to have any of those attending the course bring controversial films with them.

#### COURSE: 102

Room: 413

Period: W-3

#### GEORGE C. HENNY, M.Sc., M.D., Philadelphia, Pa.

#### Roentgen Film Characteristics and the Practical Calibration of Roentgenographic Apparatus and Processing Solutions

The characteristics of the roentgen film emulsion (together with intensifying screens if they are used), in which the roentgenologist is mainly concerned, are the "speed" and the "contrast." These characteristics are of great importance.

The "speed" determines the degree of darkening of the processed film, after standard development, for a given roentgenographic exposure and a particular anatomic part.

The "contrast," under the same conditions, determines the degree to which tissue density-differences and thickness-differences of the anatomic part will be recorded on the roentgenogram.

For uniformity of results the roentgenographic apparatus and processing solutions should be calibrated at regular intervals. Fairly simple methods of calibration, which are accurate enough for the purpose, are described and may be employed in the roentgen department without great outlay of time or money. When properly employed the roentgenograms of a given patient show uniform density from one examination to the next and the detail of the anatomic parts being studied is, as far as the film emulsion is concerned, brought out to the greatest degree.

#### SINGLE PERIOD COURSES

#### DIAGNOSTIC ROENTGENOLOGY

COURSE: 201

Room: 402

Period: F-3

V. W. ARCHER, M.D., University, Va.

# Roentgenologic Manifestations in Osteomyelitis

Negative findings early in the disease. Examples of atypical disease. Roentgenographic demonstration

of structural weakness necessitating immobilization to prevent deformity. Demonstration of sequestra and pockets as cause of draining sinuses. Brodie's abscess. Late recurrences. Differential diagnosis between osteomyelitis, lues, mycotic infection, tuberculosis, and tumor.

#### COURSE: 202

Room: 402 Period: W-3

VINCENT W. ARCHER, M.D., University, Va. F. B. BOGART, M.D., Chattanooga, Tenn.

Chest Findings in "Country Diseases"

Pulmonary findings in (1) tularemia; (2) pneumonia; (3) pleural effusion; (4) bronchitis; (5) nodular infiltration; (6) actinomycosis; (7) blastomycosis; (8) Malta fever.

#### COURSE: 203

Room: 402 Period: T-2

PAUL A. BISHOP, M.D., Philadelphia, Pa.

#### Examination and Diagnosis of Lesions of the Temporomandibular Joint

The frequency with which injuries of the temporomandibular joint are overlooked, both clinically and roentgenographically, has led to an appalling number of permanent, serious disabilities of the mandible. A technique for the roentgenographic study of this joint is presented with lantern slide demonstration of acute and chronic injuries, as well as various non-traumatic conditions.

#### COURSE: 204

Room: 401 Periods: Th-2; F-3

RALPH S. BROMER, M.D., Philadelphia, Pa.

#### The Differential Diagnosis of Skeletal Changes Occurring in Diseases of Infants and Children

The time allotted will be spent in discussing the differential roentgen diagnosis of skeletal changes occurring in diseases of infancy and childhood. All such diseases cannot be included in the time available for the course. Case material will be chosen from the following list: congenital syphilis, rickets, infantile scurvy, tuberculosis, lead poisoning, the blood dyscrasias, xanthomatosis and allied conditions, osteogenesis imperfecta, achondroplasia, multiple enchondromata, multiple cartilaginous exostoses, metastases caused by neuroblastoma, osteochondritis and endocrine disturbances. Wherever possible the early roentgen changes will be empha-

sized. The question of differential diagnosis will be approached from the standpoint of the predisposition of the various diseases to affect certain bones or certain areas of individual bones. Thus in the case of the long bones, differential roentgen signs of the disease processes in the epiphysis, the diaphysis, the metaphysis, the periosteum, cortex, etc., will be given in detail.

#### COURSE: 205

Room: 409 Period: W-2

P. F. BUTLER, M.D., Boston, Mass.

#### Consideration of Fractures from a Medicolegal Standpoint

The opinion of a roentgenologist in court must be based upon roentgenologic data, knowledge of pathology, and of the end-results of injuries. Since the question of permanent deformity and disability plays such an important part in the medicolegal evaluation of a case, special attention will be given to prognosis and the question of permanent deformity. The changes in the type of injuries since the advent of the automobile era will be discussed. The significance of certain types of skull fractures and the healing of such fractures will be considered. Particular emphasis will be placed on fractures involving the epiphyses in children and an accurate method of measuring leg length will be described.

#### COURSE: 206

Room: 408 Period: F-3

#### JOHN R. CARTY, M.D., New York City Soft Tissue Roentgenography

The pathological and anatomical basis of soft tissue roentgenography is briefly discussed, with particular reference to the newer concepts regarding fascial planes.

The essential points of the technical procedures are discussed and emphasis is placed on the necessity for an adequate understanding of the technical factors if success in this field is to be expected. Only practical aspects are to be considered, and a simple technical procedure is outlined which may be followed with the equipment found in the average roentgenographic office or department.

Following the discussion of technique the pathological conditions in the soft tissues which may be demonstrated roentgenographically are discussed and divided into appropriate groups, as follows:

Vascular Conditions: Soft tissue roentgenography is valuable in the study of arteriosclerosis and varicose veins. Information may be obtained as to whether or not the deep veins are involved. Occa-

sional valuable information may be obtained regarding arteriovenous aneurysms.

Soft Tissue Tumors: Information regarding the extent and character and whether or not the tumor is malignant may often be secured following roent-genographic examination. It is my opinion that no examination for bone tumor is complete without a soft tissue study also. Differential diagnosis between fibroid periosteal sarcoma and osteogenic sarcoma may sometimes be made. The presence of minute deposits of calcium caused by osteogenic elements in the soft tissues is the deciding factor. These calcium dots are usually entirely obliterated in roentgenograms made for bone detail. In hemangiomata distribution and location of the vessels supplying the tumor can often be ascertained. This may be of considerable value to the surgeon.

Muscle Conditions: Calcified hematomata are well shown in a soft tissue study. Occasionally a ruptured muscle may be demonstrated. Early atrophy at times may be demonstrated before there is actual reduction in size of the limb.

Infectious Conditions: Soft tissue roentgenography is invaluable in the diagnosis of gas gangrene, particularly for determining the extent of the disease. Soft tissue roentgenography is useful in the study of elephantiasis and may help in the differentiation of various types of edema. Soft tissue study of inflamed bursae is helpful, particularly where there is an absence of calcium-like material.

Soft tissue roentgenography of the larynx is briefly discussed, with special reference to carcinoma, edema and retropharyngeal abscesses.

In conclusion, the technique and scope of fasciagraphy is briefly discussed, and films shown which demonstrate its usefulness in certain selected conditions

#### COURSE: 207

Room: 406

Period: T-2

JAMES T. CASE, M.D., Chicago, Ill.

# The Roentgenologic Diagnosis of Carcinoma of the Colon

In the diagnosis of carcinoma of the colon the pathological and anatomical considerations vary according to the location of the tumor in the right or left half of the colon. In colonic polyposis the symptomatology, like the pathology, varies with the position of the tumor in the right or left colon. Special technique is a matter of utmost importance. Repetition of the examination is often necessary.

The technique of examination for and the roentgenologic manifestations of cancer of the colon will be discussed and illustrated. COURSE: 208

Room: 402

Period: F-2

#### W. EDWARD CHAMBERLAIN, M.D., Philadelphia, Pa.

# Technique and Interpretation of Oxygen Myelography

Oxygen has now been used successfully in hundreds of cases as the contrast medium for myelography. It has many advantages over other media but the roentgenographic requirements are very exacting.

Lumbar puncture vs. cisternal puncture for introduction of the oxygen; methods of increasing scope of lumbar puncture route; adaptation of ordinary conventional roentgenographic apparatus to this work; essential factors in technique; stereoscopy essential in lateral as well as dorsal projections; stereoscopic shift across long axis of spine; value of comparing lateral projections with spine in hyperflexion and hyperextension; value of "over-exposing" films; oblique projections of little value except in cervical and upper thoracic regions; suggestions for after-care of patients.

#### COURSE: 209

Room: 401

'Periods: T-2; W-2

#### ARTHUR C. CHRISTIE, M.D., Washington, D. C.

# The Diagnosis and Treatment of Bronchiectasis

History and Incidence.

Etiology and Pathogenesis.

Diagnosis.

Symptoms and signs. Necessity and means of early diagnosis. Iodized oils. Instillation of iodized oil by the passive method. Description of method. Illustrative slides to show different types of bronchiectasis and conditions which may require differential diagnosis.

Treatment.

Necessity for treating complicating inflammatory conditions. Medication. Postural drainage. Iodized oils. Bronchoscopic drainage.

Surgery: Applicability and limitations. Artificial pneumothorax. Phrenicectomy. Pneumectomy. Roentgen therapy: Rational basis for such treatment. Detailed descriptions of application, dosage, etc. Results illustrated by report of cases.

The aim of this course is to give a complete view of the diagnosis and treatment of this exceedingly common disease in which the radiologist can play an important rôle in both fields.

#### COURSE: 210

Room: 400 Period: F-2

# E. A. CODMAN, M.D., Boston, Mass. C. W. BLACKETT, M.D., Boston, Mass.

#### The Shoulder

The course will be divided into four parts:

- Normal motion of the shoulder. This portion will consist chiefly of a demonstration of the "pivotal paradox" and one must understand the explanation of this in order to appreciate the normal motion of the shoulder.
- 2. Complete roentgen examination of the shoulder. The authors will demonstrate the optimum position in which the shoulder should be exposed in order to detect any ordinary lesion of this region in which the roentgen ray helped make the diagnosis.
- 3. Pathologic conditions demonstrable by roentgen ray. This will consist chiefly of a listing of the pathologic conditions which may be demonstrable by roentgen ray. These will be amply illustrated by lantern slides and the more unusual conditions will be demonstrated.
- 4. Round table discussion. The authors hope that each person registering for this course will send to Dr. Blackett one question, as this will give them an idea of what is most desired and an attempt will be made to answer these questions during the round table discussion.

#### COURSE: 211

Room: 409 Period: Th-2

#### LEWIS GREGORY COLE, M.D., New York City

#### Pneumoconiosis

- Rapid demonstration of roentgenograms from various sources in this country and Canada, presented regardless of the extent and character of the lesion, to show the necessity of classification.
- Properly and improperly prepared autopsy specimens compared with roentgenograms.
- Dust in the lungs as observed microscopically with the light and dark fields.
- 4. Phagocytes and their effect on adjacent anatomical structures:
  - a. Black phagocytes—not destructive.
  - b. White phagocytes—destructive if over-
  - c. Black and white phagocytes—not destruc-
- Roentgenographic findings are caused by four types of pathology:
  - a. Dust flects phagocyted in clumps or streaks.
  - b. Collagen (not connective tissue) laid down

- in four patterns: whorls, lamina, gobs, and strands.
- c. Demonstration of cells and debris within the alveoli and air passages.
- d. Increased ventilation:
  - (1) Localized air cysts.
  - (2) General emphysema.
- Pathological changes in the alveolar wall, evidenced by hypertrophy, proliferation and desquamation of the alveolar lining, causing dyspnea.
- Vascular and intervascular changes in pulmonary capillaries and blood vessels, resulting in a. Avascular areas.
  - b. Hypervascular areas.
- 8. Lymph follicles are not the home of the silicotic (?) nodule. It is more free of pathology than any other structure in the lung.
- Four types of pneumoconiosis constitute different pathological entities and different compensation problems.
- 10. Philosophy: And so, what? The application of these findings to a solution of the pneumoconiotic (silicotic) problem.

#### COURSE: 212

Room: 401 Period: W-3

#### HOWARD P. DOUB, M.D., Detroit, Mich.

#### The Invertebral Disc

This discussion will be limited as much as possible to the disc itself, but owing to its intimate relationship to the vertebrae, it will be necessary to consider the spine to some extent.

We wish to present the anatomy of the disc and its vascular supply together with reference to defects in its development which often lead to abnormalities in later life. Changes in the fibrous structure and in the cartilage plates, due either to disease or trauma, will be brought out. The effect of these changes on the vertebral column as a whole will then be considered.

The relationship of the disc to spinal deformities, such as the arthritides, kyphoses, tumors and injuries will also be discussed.

#### COURSE: 213

Room: 403 Period: T-2

#### C. G. DYKE, M.D., New York City

#### The Normal Encephalogram and Ventriculogram

This seminar will deal with the history of pneumoencephalography, the indications and contraindications for the procedure, the reactions to the test, the preparation of the patient, and the roentgen technique. The discussion of the above subjects will be followed by a thorough roentgen study of the lateral ventricles, the basal cisterns and the cortical markings, and also the structures which bound them. The demonstration will be illustrated.

### COURSE: 214

Room: 403 Periods: W-2; Th-2

C. G. DYKE, M.D., New York City

# Pneumo-encephalographic Diagnosis of Brain Tumor

This period will be devoted to an enumeration of the criteria used in the diagnosis of the various types of intracranial tumors. The characteristic changes produced by some of the neoplasms will be emphasized. The demonstration will be fully illustrated.

#### COURSE: 215

Room: 408 Period: T-2

PEDRO L. FARIÑAS, M.D., Havana, Cuba

# Bronchographic Examination in Primary Bronchogenic Carcinoma

Description of technique.

Bronchographic aspects of the infiltrating and polypoid types of tumors.

Comparison between the bronchographic alterations and the anatomical specimen in the different types of bronchial tumors.

#### COURSE: 216

Room: 409 Period: T-2

JOHN T. FARRELL, JR., M.D., Philadelphia, Pa.

# Roentgen Diagnosis of Lesions of the Esophagus

The technique of roentgen examination of the esophagus with liquids, semi-solids, and solids, together with the indications and limitations of each, will first be presented. This will be followed by consideration of the roentgen anatomy and physiology. Study of pathological states will embrace the diagnosis and differential diagnosis of congenital, inflammatory, traumatic, functional, and neoplastic conditions of the organ.

COURSE: 217

Room: 402 Period: W-2

A. O. HAMPTON, M.D., Boston, Mass.

## Iodized Oil Myelography in the Diagnosis of the Prolapsed Intervertebral Disc

This course will deal chiefly with the diagnosis of ruptured intervertebral discs. The technique of examination, the sources of error and the mechanism of the filling defects produced by these lesions will be illustrated. Comparisons will be made between iodized oil myelography and air myelography in the diagnosis of ruptured discs.

### COURSE: 218

Room: 401 Period: F-2

PAUL C. HODGES, M.D., Chicago, Ill.

# Further Developments in Roentgen Pelvimetry and Fetometry with Special Reference to Orthometric Reproduction

The indications for roentgen pelvimetry and fetometry, the technique of making the measurements, and the application of the measurements to clinical obstetrics will be considered. Models, specimens, charts and roentgenograms will be demonstrated. Opportunity will be given for questions and discussion.

### COURSE: 219

Room: 409 Period: F-2

### B. R. KIRKLIN, M.D., Rochester, Minn.

# Roentgenologic Appraisal of Results Following Operations on the Stomach and Duodenum

When surgical operations have been performed on the stomach and duodenum, roentgenologic examination is often solicited to determine whether satisfactory results have been obtained, or whether the original disease has recurred, or whether new complications have developed. Manifestly this field of diagnosis is difficult, for surgical techniques vary considerably both from choice and from necessity. Nevertheless, examination with the roentgen ray is the most readily available and most reliable method of exhibiting and appraising postoperative conditions. Accordingly, in this course of instruction the following subjects will be discussed in detail:

Preliminary information that should be given the roentgenologist—character of operation, disease for which it was performed, time that has elapsed since operation.

Technique of examination. Differences between early and late results. Satisfactory results from the various operations including gastrojejunostomy,

Billroth I, Billroth II, Polya, Roux, total gastrectomy, sleeve resection, local resection, pyloroplasty, gastroduodenostomy, entero-enteroseomy.

Operations that appear roentgenologically to be most satisfactory in their mechanical and functional results.

Unsatisfactory results from operation. Complicating lesions including gastrojejunal ulcer, gastrojejunitis, gastro-jejuno-colic fistula and recurring ulcer.

### COURSE: 220

Room: 403 Period: W-3

# KARL KORNBLUM, M.D., Philadelphia, Pa.

### Tumors about the Sella Turcica

The roentgen examination of the head with special reference to the sella turcica, emphasizing particularly the need of careful roentgenographic technique. The anatomy of the region of the sella turcica will be given and attention directed to the cardinal changes produced by tumors in its vicinity. The characteristic deformities occurring in the intrasellar, suprasellar and parasellar tumors and neoplasms arising in the sphenoid sinus will be considered.

### COURSE: 221

Room: 406 Period: Th-2

### A. S. MACMILLAN, M.D., Boston, Mass.

### Roentgen Examination of the Accessory Nasal Sinuses

The technique of examination of the patient for suspected sinus disease will be considered. Particular stress will be placed upon four positions which the instructor considers the irreducible minimum in the examination of the sinuses.

Acute and chronic sinusitis, the sinus involvement in allergy and in malignant disease as well as the cause of exophthalmus in sinus involvement.

There is a great deal of discussion among otolaryngologists as to the value of the roentgen ray as an aid in the diagnosis. At attempt will be made to talk about the practical points in interpretation.

### COURSE: 222

Room: 406 Period: F-3

# A. S. MACMILLAN, M.D., Boston, Mass.

### Roentgen Examination of the Mastoids

The technique of the examination of the patient for mastoid involvement in acute infections of the middle ear will be considered. Demonstrations of the various positions for the examination of the petrous pyramid in the search for involvement of this area as a complication of infection and invasions by new growths of the base of the skull and nasopharynx.

He will consider the rôle played by the roentgen ray in the determining of the optimum time for operation, the limitations of this type of examination and the need for the roentgenologist to acquaint himself with the problems of the surgeon.

## COURSE: 223

Room: 414 Period: Th-2

# B. H. NICHOLS, M.D., Cleveland, Ohio Diagnosis of Renal Tumors

This instruction course will consist of a classification of renal tumors with a discussion of many of their clinical features which might lead to the supposition of the presence of such a lesion. There will also be presented the characteristic roentgen findings in the various types of tumors, together with lesions simulating renal tumors, with their differential diagnosis.

### COURSE: 224

Room: 408 Period: Th-2

# CARLETON B. PEIRCE, M.D., Montreal, Canada

# Bronchographic Technique with Demonstration of the Anatomy and Pathologic Changes of the Bronchial Tree

The preparation of the patient for bronchography, the apparatus used and the various techniques for instillation of iodized oils will be demonstrated and discussed briefly.

Major emphasis will be placed on the demonstration of the topography of the normal bronchial tree, the localization and diagnosis of pathologic changes of the trachea and bronchi.

### COURSE: 225

Room: 406 Period: W-3

# JOHN W. PIERSON, M.D., Baltimore, Md.

### Bone Changes in Lymphoblastomata

The roentgenological study of the skeletal manifestations of the lymphoblastomata is of interest because the bone changes assume so many and such varied forms. In some cases gross deformities of bone are produced, while in others the changes are so minimal that they are extremely difficult to detect.

This great variety of changes renders the differential diagnosis exceedingly difficult, because many other conditions are imitated. A review of the pathological background offers a logical explanation for the changes depicted by roentgen examination.

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The gross changes are easy to demonstrate but signs of early involvement of the bones are extremely difficult to detect. Success in the demonstration of minimal changes can only be obtained by painstaking efforts in which a very precise technique is employed. Such a technique will be discussed and its results demonstrated.

### COURSE: 226

Room: 403

Period: F-2

# LEO G. RIGLER, M.D., Minneapolis, Minn. Roentgen Diagnosis of Pleural Effusions

The anatomy, physiology and physical characteristics of the pleura and pleural space will be reviewed. The importance of these factors in the roentgen consideration of pleural collections will be emphasized. Early diagnosis and differential diagnosis of fluids in the pleural cavity, free and encapsulated, will be reviewed. The differential findings exhibited by exudates and transudates and encapsulated collections will be demonstrated. Roentgenologic findings in pneumothorax and its complicated aspects such as adhesions, encapsulations, fluid and mediastinal hernia will be detailed. The technique of the roentgenoscopic and roentgenographic examination of the pleural cavity for disease will be considered.

### COURSE: 227

Room: 403

Period: F-3

# SAMUEL A. ROBINS, M.D., Boston, Mass. Utero-salpingography

This course concerns itself with the roentgen examination of the uterus and tubes by means of opaque media. The subject will be discussed under the following headings: (1) history; (2) apparatus and technique; (3) opaque media; (4) indications; (5) normal morphology; (6) physiologic variations; (7) pathologic variations; (8) pregnancy; (9) tumors (fibroids, polypi, malignancy); (10) inflammatory changes of the tubes; (11) tubal pregnancy; (12) sterility; (13) post-therapeutic changes in the uterus; (14) contraindications; (15) dangers.

Lantern slides of various physiologic and pathologic conditions of the uterus and tubes will be shown to evaluate this method of examination.

# COURSE: 228

Room: 405

Period: W-3

L. R. SANTE, M.D., St. Louis, Mo.

Bronchial Occlusion

Tracheal obstruction
Roentgen manifestations and causes

Complete bronchial obstruction resulting in atelectasis: massive type from obstruction of main stem bronchus; lobar form from occlusion of larger bronchial branches; lobular form resulting from occulusion of smaller bronchial subdivisions.

The causes and conditions which give rise to these various types of bronchial occlusion; their association with other conditions and diseases such as aspiration of foreign body, trauma, pulmonary tuberculosis, bronchogenic tumor, post-operative nhibition, general debility, weakness, etc.

Incomplete bronchial occlusion resulting in obstructive emphrsema: massive involvement of entire lung (Marges' sign), smaller bronchial subdivisions, bronchiectasis and pseudobronchiectasis from partia bronchial obstruction by foreign body of long sojcurn and from bronchogenic tumor.

### COURSE: 229

Room: 407

Periods: W-3; F-3

## RICHARD SCHATZKI, M.D., Boston, Mass.

### Roemgen Diagnosis of Gastritis

Over-emphasis and marked criticism characterize the present at itude towards roentgen diagnosis of gastritis. This zourse tries to evaluate critically our knowledge at this time. Its emphasis is laid upon the practically important features connected with the diagnosis and cifferential diagnosis of gastritis, and not on theoretical considerations. The reasons why, in spite of the progress of gastroscopy, gastritis is still a problem for everyday roentgenology will be illustrated.

The round table discussion will include the following questions:

General principle and technique of the gastric relief demonstration; roentgen findings in some types of gastritis; critical discussion of the possibilities and limitations in regard to roentgenological diagnosis of gastritis; differential diagnosis.

### COURSE: 230

Room: 410

Period: Th-2

# W. H. STEWART, M.D., New York City FRANK HUBER, M.D., New York City

### Lesions of the Lower Esophagus and Cardiac Portion of the Stomach

A discussion of the recognition and differential diagnosis of lesions of the lower esophagus and cardiac portion of the stomach.

Carcinoma, diverticula, cardiospasm, peptic ulcer, varices, diaphragmatic hernia, congenitally short esophagus, as wel as carcinoma and diverticula of the cardiac portion of the stomach will be discussed

and illustrated. In addition to the examples showing characteristic involvement, films will be shown of atypical lesions offering unusual diagnostic difficulties.

The presentation will include an outline of the positions and technique necessary to obtain diagnostic films as well as some discussion of therapeutic procedures.

### COURSE: 231

Room: 414 Period: W-2

M. S. STROCK, D.M.D., Boston, Mass.

### Analysis of Dental Roentgenograms as an Aid in the Recognition of Systemic Disease

This seminar will correlate dental findings as seen in the regular dental film with systemic disease, particularly with disorders of the calcium and phosphorus metabolism. An effort will be made to show from dental films the everyday pathology as well as some of those diseases which, though rare, manifest themselves in the mouth. Particular attention will be given to hyperparathyroidism and hypoparathyroidism and their oral manifestations. The need for accurate dental findings will be pointed out, yet an attempt will be made to keep the description of findings sufficiently brief to be of value in the hospital.

### COURSE: 232

Room: 400 Periods: W-3; F-3

# PAUL C. SWENSON, M.D., New York City Neoplasms of the Small Intestine

The incidence and character of the various benign and malignant neoplasms of the small intestine, including those of the duodenum, will be discussed. The roentgenologic manifestations of these lesions will be presented, and the technique of examination, including the use of the Miller-Abbott tube, will be described in detail.

### COURSE: 233

Room: 407 Period: F-2

### KURT H. THOMA, D.M.D., Boston, Mass.

### Changes in the Jaws caused by Skeletal Diseases and Tumors

The roentgen and pathologic findings of various lesions of the jaw will be shown, and the clinical findings will be described. The proper roentgen method for lesions located in various parts will be discussed. The following diseases will be considered:

- 1. Fractures of the jaws.
- 2. Diseases of the mandibular joint.
- 3. Skeletal diseases: cretinism, acromegaly, hy-

- perparathyroidism, osteitis deformans, Schüller-Christian's disease, osteoselerosis fragilis generalisata.
- 4. Localized diseases: oxycephaly, leontiasis ossea, atrophy, hemiatrophy, osteomyelitis, irradiation osteomyelitis, syphilis.
- 5. Cysts of the jaws: facial cleft cysts, incisive canal cysts, odontogenic cysts, traumatic cysts.
- Odontogenic tumors: adamantinomoblastoma, odontoma, cementoma.
- Osteogenic tumors: exostosis (torus palatinus), osteoma, chondroma, myxoma, osteogenic sarcoma.
- 8. Central tumors of non-odontogenic and non-osteogenic origin: fibroma and fibrosarcoma, angioma, Ewing's tumor, multiple myeloma, primary carcinoma, and tumors metastatic to the jaws.

#### COURSE: 234

Room: 406 Period: F-2

EDWARD C. VOGT, M.D., New Bedford, Mass. GEORGE M. WYATT, M.D., Boston, Mass.

### Chest and Heart Diseases in Infants and Children

We arbitrarily divide our patients into two age periods, namely, infants from birth to two years, and children from two years to twelve, because there is a certain age incidence in the diseases encountered. Also because certain diseases, such as tuberculosis, are less easily differentiated in early years of life. Diseases of congenital origin are more likely encountered in the infant. This is particularly true of heart disease. Using lantern slide illustrations we will discuss with as much detail as our time permits the different disease conditions, primary and secondary, congenital and acquired, that affect the heart, lungs, pleura, mediastinum and thorax.

### COURSE: 235

Room: 407 Periods: T-2; W-2

# W. WALTER WASSON, M.D., Denver, Colorado

# The Nasal Accessory Sinuses of Infants

This presentation has to do particularly with aeration of the nasal accessory sinuses of infants after delivery. This clearing process is a definite physiological one and has many variations. Improper clearing soon becomes a pathologic condition and a basis for future sinus infections. These sinus infections definitely influence the entire respiratory tract.

COURSE: 236

Room: 406 Period: W-2 Room: 410 Periods: W-3; F-3

# HARRY M. WEBER, M.D., Rochester, Minn.

# Lesions of the Colon Frequently and Easily Overlooked

Advanced pathologic processes occurring in the large intestine usually produce relatively marked morphologic changes in the part of the intestine affected, and so are discovered without great difficulty at roentgenologic examination. Certain clinically important lesions, however, never become large, or produce alarming symptoms even when small, or are encountered so early in their development that very obvious morphologic changes have not as yet taken place, and thus are easily overlooked at roentgenologic examination. This discussion will be limited to the roentgenologic diagnosis of small neoplastic lesions of the large intestine, and to those roentgenologically recognizable changes which signify the earliest manifestations of certain important non-neoplastic lesions of this division of the alimentary tract. The conduct of the roentgenologic examination of the large intestine will be reviewed briefly, and advantages and limitations of the various diagnostic procedures currently used in this field will be discussed in considerable detail.

### SINGLE PERIOD COURSES

### THERAPEUTIC RADIOLOGY

COURSE: 301

Room: 410 Period: T-2

> ARTHUR U. DESJARDINS, M.D., Rochester, Minn.

# Lymphoblastoma (Hodgkin's Disease, Lymphosarcoma and Leukemia)

Prominent clinical features of Hodgkin's disease and lymphosarcoma; presenting symptoms and their relative importance; involvement of mediastinal nodes; involvement of retroperitoneal nodes; involvement of other nodes; extranodular infiltration; involvement of skin; great variation in complications; pathology; condition of the blood; treatment in relation to anatomic distribution of the disease and of its complications; quantity and quality of rays; variations in radiosensitiveness and reasons therefor; effect on the blood cells; repetition of treatment and factors which should govern it; prognosis; factors governing survival.

# RICHARD DRESSER, M.D., Boston, Mass.

COURSE: 302

### Roentgen and Radium Therapy

This course will be prefaced by a brief résumé in simple terms of the physical principles of radiation. The effect of voltage, filtration, distance, etc., in roentgen-ray production will be discussed. The relative merits o various methods of radium application will be taken up.

The radiobgical management and end-results in the more common types of malignant disease will be discussed. Special attention will be given to cancer of the skin, lip, mouth, larynx, breast, uterus, bladder, and prostate.

The advan ages and limitations of roentgen rays produced at voltages greater than 200,000 will be given brief consideration.

### COURSE: 303

Room: 405 Period: T-2

E. C. ERNST, M.D., St. Louis, Mo.

### Practical Concepts of Radiation Treatment of Carcinoma of the Cervix Uteri

The practical irradiation management of carcinoma of the carvix will be discussed both from the standpoint of the institutional tumor clinic and the private office procedure. Although realizing that the radiation treatment standards continue to remain somewhat in a state of flux and that individualization in the application of roentgen rays and radium is a most essential consideration, nevertheless certain fundamental concepts in our routine procedures are most helpful in the management of cancer of the cervix. These and many other practical therapeutic considerations, including external roentgen therapy, intracavity radium and roentgen methods of treatment and the do-age measurement problems, will be discussed and illastrated.

### COURSE: 304

Period: F-3 Room: 413

# G. FAILLA, D.Sc., New York City Some Aspects of Radiosensitivity

Variation of radiosensitivity with cell type, stage of development, e.c.

Influence of circulation on cell reaction to radiation in accordance with author's theory of the biological action of onizing radiations. Experimental findings tending to support theory.

Relative radiose sitivity of normal and pathological tissues most in portant factor in radiation therapy. Ways in which radiosensitivity ratio may be improved. Possible influence of wave length on this ratio.

Applications to some practical problems.

### COURSE: 305

Room: 413 Period: F-2

# ROBERT E. FRICKE, M.D., Rochester, Minn.

# Radiation Therapy for Carcinoma of the Rectum

Carcinoma of the rectum presents many problems not encountered in malignant disease elsewhere in the body. In early stages it is best handled surgically. However, very few rectal lesions are diagnosed in an early stage. Radiation therapy has a major rôle in this disease in close conjunction with surgical measures. For the past several years between 100 and 200 patients with carcinoma of the rectum have received radium therapy each year at the Mayo Clinic, some postoperatively, a few preoperatively, and the majority with advanced inoperable lesions were treated with palliation in mind. Results of treatment have been definitely encouraging. Roentgen therapy has been helpful in selected cases.

Newer methods of radiation treatment will be described. The microscopic grade of the cancer, its location, the presence or absence of metastasis and the general condition of the patient all have an important bearing on the selecting of the type of treatment. Topical or contact therapy and interstitial treatment with needles or seeds will be described. The advantages and disadvantages of colostomy will be mentioned. Results of treatment will be given and a discussion of the value of the palliation offered by treatment in inoperable cases. At the present time radiation therapy has a major rôle in the palliative treatment of extensive inoperable lesions; in the future I believe preoperative therapy will prove even more successful and applicable in the management of these serious conditions.

### COURSE: 306

Room: 414 Period: F-2

# OTTO GLASSER, Ph.D., Cleveland, Ohio U. V. PORTMANN, M.D., Cleveland, Ohio

# Dosage Measurements with the Thimble Chamber in Practice

The historical development of thimble chamber dosimeters, their calibration in roentgens, the measurement of quantity and quality, depth dose and back-scattering in phantoms will be discussed. The difference between the thimble chamber dosimeters and other types of dosimeters will be discussed. Likewise, the clinical applications of the thimble chamber will be discussed.

### COURSE: 307

Room: 412 Period: T-2

# GEORGE W. GRIER, M.D., Pittsburgh, Pa.

# Treatment of Superficial Malignant Neoplasms

A general outline of the technique which the author has used for treatment of superficial malignant neoplasms since the advent of the Coolidge tube will first be given.

Variations in technique for lesions in different locations and different types of involvement will be discussed. Also, variations which are necessary in different types of malignant disease.

The actual application of masks and special applicators which may be necessary in difficult locations will be demonstrated.

Lesions of the lip and mouth will be included.

Abstracts of actual case histories with illustrative lantern slides will be presented for each type of lesion described.

### COURSE: 308

Room: 408 Period: F-2

# ARTHUR U. DESJARDINS, M.D., Rochester, Minn.

### Roentgen Treatment of Inflammatory Conditions

This instructor will discuss the roentgen treatment of the following conditions: furunculosis, carbuncle, granuloma, erysipelas, gas bacillus infection, mastoiditis, sinusitis, osteomyelitis, some fungus infections, various localized types of cellulitis, infected rhinophyma, bronchiectasis, etc. The dosage and technique will be discussed in detail.

### COURSE: 309

Room: 408 Period: W-2

# H. DABNEY KERR, M.D., Iowa City, Iowa

# Roentgen Irradiation of Deep Pelvic Malignant Tumors, Particularly Carcinoma of the Cervix

Although standardized methods of treatment are valuable, it is important to know what is actually being delivered to the lesion, and the response, if we are to make any real advance in our irradiation of pelvic neoplasms. This will be a discussion of the method used in the treatment mainly of carcinoma of the cervix at the University of Iowa. Where possible this consists of the use of nine portals about the pelvis and, in addition, either radium or transvaginal roentgen irradiation according to the method advocated by Merritt and by Erskine. The question of doses delivered to the parametrial extensions and the primary lesion will be discussed in relation to daily dosage division and cumulative dose. An attempt

will also be made to correlate delivered dose with clinical result.

#### COURSE: 310

Room: 412 Periods: W-3; F-3

## MAURICE LENZ, M.D., New York, N. Y.

# Roentgen Therapy of Cancer of the Larynx and Pharynx

Roentgen therapy of cancer of the larynx and pharynx is influenced by the clinical character, anatomical extent and location, accessibility, invasion of cartilage or bone, infection, ability of the patient to tolerate radiotherapy, and inherent radiosensitivity of the tumor. Technique of treatment also has an important bearing upon prognosis.

All the patients with cancer of the larynx and pharynx treated in the Radiotherapy Departments of Presbyterian Hospital and Montefiore Hospital, New York City, between 1926 and 1939 (approximately 250 cases) have been analyzed in an effort to clarify the relative importance of the factors just mentioned. This analysis, together with data in the literature, forms the basis of this informal discussion. It is hoped that a free interchange of views on details of the problem will take place between lecturer and audience during the course.

# COURSE: 311

Room: 414 Periods: W-3; F-3

# T. LEUCUTIA, M.D., Detroit, Mich.

# Radiation Therapy of Bone Tumors

- (1) Osteogenic sarcoma. Radiation therapy is used in association with surgery in pre- or postoperative form in all types, except the pure osteolytic type, in which it is used alone. In the inoperable group, irradiation produces definite symptomatic relief. The five year survival for the entire series amounts to 17 per cent.
- (2) Giant cell tumor. Here radiation therapy is the method of choice. There are two requisites: (a) irradiation must be carried out with gradually decreasing doses for nearly two years, and (b) a limited use of the affected bone must be made so as to prevent marked demineralization from disuse. The final results are, with few exceptions, good.
- (3) Ewing's tumor. In the very early cases, radiation therapy may lead to occasional five year survival; in the others, only palliation is obtained, although the immediate response is often striking.
- (4) Multiple myeloma. Radiation therapy leads to limited symptomatic relief, but no cure is possible.
- (5) In the group of benign tumors, radiation therapy is of definite value in chondroma, myxoma, hemangioma, cystic conditions, etc.

The detailed procedure is presented in the various groups and the technique of irradiation illustrated. Final statistical data are included.

### COURSE: 312

Room: 410

Period: F-2

# CHARLES L. MARTIN, M.D., Dallas, Texas

## Complete Care of Cancer of Mouth and Lip Including Cervical Metastases with Irradiation Alone

A plan for the complete radiological care of all stages of cancer of the mouth and lip will be described. Although both radium and roentgen rays are used, the equipment is relatively inexpensive and the time of treatment is short. Much emphasis will be placed on the intensive irradiation of metastatic cervical glands, using a combined roentgen-ray and interstitial radium technique which has yielded some very promising results. Detailed descriptions of the procedure used in a number of actual cases have been prepared for presentation.

### COURSE: 313

Room: 405

Periods: Th-2; F-2

# E. A. MERRITT, M.D., Washington, D. C.

### Technique of Treatment of Cancer of the Cervix and Results Therefrom

This presentation is intended neither as a lecture nor as an instruction course; however, it embraces a complete description of a technique covering the radiation treatment of all stages of carcinoma of the cervix uteri.

The advantages of roentgen over radium therapy will be emphasized and a method of treating the cancerous cervix through specially designed specula will be described.

Hospitalization of the patient is rarely necessary, infection is reduced to a minimum; anesthetics and surgical trauma of the cervix completely avoided; severe roentgen sickness and undue skin reactions almost completely controlled.

It provides the radiologist with a standardized technique which will facilitate future statistical comparisons, and divorces therapy of cancer of the cervix from all of the unnecessary and expensive surgical procedures and dangers associated with the use of radium.

Lantern slides, a wax model, and specula employed will serve to clearly demonstrate the method in actual operation.

Results covering a three year period will be stated.

COURSE: 314

Room: 412 Period: F-2

# COURSE: 317

# riod: F-2 Room: 402 Period: Th-2

# WILLIAM S. NEWCOMET, M.D., Philadelphia, Pa.

# Radium Therapy of Hemangiomata

Early methods used in the treatment of hemangio-

The application of roentgen and radium radiation, the differences between them.

Varieties of hemangiomata from the standpoint of the pathologist, dermatologist, surgeon and radiologist.

Possibility of malignant degeneration in those treated by irradiation and those of unknown origin, in youth and adult life.

Spontaneous ulceration and ulceration occurring during treatment. Other complications, local lack of growth, dermatitis local and general, telangiectasis and lack of function of affected part.

Discussion of treatment in the young infant, child and adult.

General review of groups and individual cases; with emphasis upon unusual bone changes observed in different types.

Results observed immediately after treatment and ten to twenty years later.

### COURSE: 315

Room: 405 Periods: W-2; F-3

### G. E. PFAHLER, M.D., Philadelphia, Pa.

### Radiation Treatment of Cancer of the Breast

The technique for the treatment of cancer of the breast cannot be standardized. The treatment will be demonstrated for cancer of the breast in various stages, including positioning of patient for treatment.

There will also be a demonstration of some of the cases treated primarily and completely by irradiation, also preoperative and postoperative irradiation, including the management of recurrences.

### COURSE: 316

Room: 414 Period: T-2

# U. V. PORTMANN, M.D., Cleveland, Ohio

# The Thyroid Gland, Its Anomalies and Diseases

The embryology, anatomy and physiology of the thyroid gland will be discussed in relationship to the etiology and treatment of pathological conditions such as anomalies, diseases attributed to dysfunction and neoplasms.

# DOUGLAS QUICK, New York City

# Treatment of Metastatic Cervical Nodes from Primary Epidermoid Carcinoma of the Upper Mucous Membrane Tract

The problem will be considered under the following headings:

- General considerations leading up to the present plan.
- 2. External irradiation, its place, and technical manner of delivery.
- 3. Surgical dissection of the neck.
- 4. Interstitial irradiation, preferential method, and technique.
- 5. Palliative therapy.

#### COURSE: 318

Room: 408 Period: W-3

# EDITH H. QUIMBY, M.S., New York City Artificial Atomic Disintegration

This course will be essentially a general descriptive outline of methods of producing atomic disintegration, and of the products thus obtained. Neutrons and artificially radioactive substances will be discussed in some detail. Brief mention will be made of various biological and clinical uses to which these materials have been put, up to the present time.

# COURSE: 319

Room: 410 Period: W-2

# GORDON E. RICHARDS, M.D., Toronto, Canada

# The Treatment of Carcinoma of the Tongue

The material for this course is based on a careful study of approximately 200 cases of carcinoma of the tongue in which the primary lesion has been treated by irradiation. The irradiation procedures have included radium in a variety of forms from weak seeds to teleradium therapy with a 4 gram radium bomb, and roentgen therapy at all voltages from the Chaoul method to 400 kv. therapy. Complications have been treated both by irradiation and by combinations of surgery and radiotherapy. The cases are thoroughly worked up and certain decisions have been reached which have been agreed to by surgical consultants. The results in this series of cases are distinctly encouraging and I think we are in a position to make quite definite statements on most of the important problems which arise in treating carcinoma of the tongue.

The group of cases of carcinoma of the buccal mucosa is smaller. These cases have also been carefully worked up and here, likewise, we have reached conclusions which are encouraging and are somewhat at variance with present day teaching regarding this disease.

### COURSE: 320

Room: 413 Period: T-2

### K. W. STENSTROM, Ph.D., Minneapolis, Minn.

# Characteristic Roentgen Radiation and Absorption

I. Introduction:

Wave length of roentgen rays. Spectrometric analysis of a roentgen-ray beam. Graphic representation of the continuous spectrum. Consideration of photons, quanta. The atomic structure.

- 2. Characteristic radiation produced in the target of the roentgen tube.
- Groups of spectral lines from tungsten, K, L, M lines.
- Characteristic radiations from the different elements and their correlation with atomic numbers.
- 5. Absorption of roentgen rays by atoms.
- 6. Characteristic absorption.
- Characteristic radiation produced by roentgen rays.
- 8. Selection of secondary filters.

## COURSE: 321

Room: 413 Period: Th-2

# ROBERT B. TAFT, M.D., Charleston, S. C.

# Dosage Measurement from a Clinical Standpoint

The author proposes to describe briefly and show photographs of all the methods in use today for roentgen-ray measurement, stating the advantages and disadvantages of each. Illustrations should be obtainable from manufacturers, which will be shown as lantern slides. The value of the "roentgen" as a clinical unit will be discussed and mention of the proposed unit, the "duane" will be made. Pros and cons for the direct dosage measurement on the skin of the patient throughout the treatment time will be given. Air measurements versus skin measurements will be outlined and tables given for back-scattering at commonly used wave lengths. Half of the period will be taken up with the above and round table discussion will follow. Throughout all, an earnest effort will be made to keep the matter within the scope of the clinical radiologist who has little knowledge of, or interest in, pure physical measurements. The author, having had some experience in both clinical and

physical work, will attempt to narrow the far-too-wide gap between the clinician and physicist. A typed summary will be available to those attending.

### COURSE: 322

Room: 413

Period: W-2

# LAURISTON S. TAYLOR, Ph.D., Washington, D. C.

# The Measurement of Quantity and Quality of Roentgen Rays

A general discussion, aimed at showing the necessity for roentgen-ray quantity and quality measurements, will be presented. A brief outline of the fundamental principles involved in the application of roentgen-ray standards will be given. A few examples of actual cases involving the application of physical dosage measurement will be carried through. Likewise the method of determining an absorption curve will be illustrated and the information obtainable therefrom discussed. No discussion of tissue dosage or related subjects will be given.

### COURSE: 323

Room: 412

Period: W-2

# CHARLES A. WATERS, M.D., Baltimore, Md.

### Radiation Treatment of Renal Tumors

The author will discuss (1) a brief differential diagnosis of renal tumors as related to roentgen diagnosis and treatment; (2) previous statistics on the curability of renal tumors without the aid of preoperative irradiation; (3) the immediate effects of radiation upon the various types of renal tumors; (4) the dangers, pitfalls, and contraindications of irradiation; (5) a discussion of elapsed time between the radiation therapy and operative removal, and (6) the results in preoperative irradiated cases as compared to non-preoperative irradiated cases.

### COURSE: 324

Room: 407

Period: Th-2

# J. L. WEATHERWAX, M.S., Philadelphia, Pa. Radium Dosage

A brief discussion of the disintegration cascade of radium; active deposit; differentiation of radium compared to radium emanation or radon; absorption by different filters and thicknesses of filter; half-life and average life of radon; types of radium applicators; interstitial irradiation; expression of dosage in terms of milligram-hours, millicuries-destroyed and a discussion of an attempt to express dosage in roentgens.

An outline will be furnished with a bibliography.

COURSE: 325

Room: 409 Periods: W-3; F-3

# B. P. WIDMANN, M.D., Philadelphia, Pa.

# Radiation Therapy in Cancer of the Skin

Technical procedures for the radium and roentgen treatment of cancer of the skin will be reviewed and analyzed in detail. A definite predetermined plan of dosage has been formulated according to the estimated surface area and thickness of the lesion. Special emphasis will be placed on the value of low volt-

age roentgen rays (100–135 kv.), and a clinical comparison with radium will be made according to a great variety of patterns for single and multiple radium tubes with different sizes of fields, filters and distances. Conclusions will be drawn from a large clinical experience with massive and fractional doses. Determinations of the "maximum safe dose," the "minimal effective dose," the daily intensity and the probable best rate of administration will be considered with specific recommendations aft a routine experience demonstrating results and skin tolerance.

		2 00 4 2 50	Code: Ti
Code: T-1	1st PERIOD-		Code: T-1
SL-1Warren.	Special Lecture: Radios	sensitivity of Tumors	
Code: T-2	2nd PERIOD-	-3:00 to 4:15	Code: T-2
Diagnostic Roentgenology		Therapeutic Radiology and Sequential Courses	
	Examination and Diagnosis of	A-Murphy	Bone Tumor Conference
203—Bishop	Lesions of Temporomandib- ular Joint	301—Desjardins	Lymphoblastoma
207—Case	Roentgenologic Diagnosis of Cancer of the Colon	303—Ernest	Radiation Treatment of Can cer of the Cervix
209—Christie	Diagnosis and Treatment of Bronchiectasis	307—Grier	Treatment of Superficia Malignant Neoplasms
	Normal Encephalogram and Ventriculogram	316—Portmann	The Thyroid Gland
213—Dyke		320—Stenstrom	Characteristic Roentgen Ra
215—Fariñas	Bronchographic Diagnosis of Primary Bronchogenic Car- cinoma		diation and Absorption
216—Farrell	Roentgen Diagnosis of Lesions of the Esophagus		
235—Wasson	Nasal Accessory Sinuses of Infants		

# 'CONDENSED SCHEDULE OF COURSES ON WEDNESDAY

Code: W-1 1st PERIOD-2:00 to 2:50 Code: W-1

SL-2....Schnelle......Special Lecture: Roentgen Rays in Veterinary Medicine

Code: W-2 Code: W-2 2nd PERIOD-3:00 to 4:15

Diagnostic Roentgenology		Therapeutic R Sequentia	
205—Butler	Fractures from their Medico-	A—Murphy	Bon
209—Christie	legal Standpoint  Diagnosis and Treatment of	309—Kerr	Roe
	Bronchiectasis Pneumo-encephalographic	315—Pfahler	Rad
214—Dyke  217—Hampton	Diagnosis of Brain Tumors  Iodized Oil Myelography in Diagnosis of Protruded In-	319—Richards	Trea th M
231—Strock	Analysis of Dental Roentgen- ograms as Aid in Recogniz-	322—Taylor	Mea ar R
235—Wasson	ing Systemic Disease  Nasal Accessory Sinuses of Infants	323—Waters	Rad na
236—Weber	Lesions of the Colon Easily and Frequently Overlooked		

A—Murphy	Bone Tumor Conference
309—Kerr	Roentgen Treatment of Deep Pelvic Neoplasms
315—Pfahler	Radiation Treatment of Cancer of the Breast
319—Richards	Treatment of Carcinoma of the Tongue and Buccal Mucosa
322—Taylor	Measurement of Quantity and Quality of Roentgen Rays
323—Waters	Radiation Treatment of Re- nal Tumors

#### Code: W-3 3rd PERIOD-4:30 to 5:45

202—Archer Bogart	Chest Findings in "Country Diseases"
212 <b>—D</b> oub	The Intervertebral Disc
220—Kornblum	Tumors about the Sella Tur-
225—Pierson	Bone Changes in Lympho- blastoma
228—Sante	Bronchial Occlusion
229—Schatzki	Roentgen Diagnosis of Gas- tritis
232—Swenson	Neoplasms of the Small Intestine

# Therapeutic Radiology and Miscellaneous Courses

Code: W-3

102—Henny	Roentgen Film Character- istics and Calibration of Apparatus and Developing Solutions		
302—Dresser	Roentgen and Radium Therapy		
310—Lenz	Roentgen Therapy in Cancer of the Larynx and Pharynx		
311—Leucutia	Radiation Therapy in Tumors of Bone		
318—Quimby	Artificial Atomic Disintegration		
325—Widmann	Radiation Therapy in Cancer of the Skin		

'	CONDENSED SCHEDULE O	F COURSES ON T	HURSDAY	
Code: Th-1	1st PERIOD-	-2:00 to 2:50	Code: Th-1	
	SL-3Castle	.Special Lecture: Leu	ıkemia	
Code: Th-2	2nd PERIOD	-3:00 to 4:15	Code: Th-2	
Diagnostic Roentgenology			adiology, Miscellaneous quential Courses	
	Differential Diagnosis of Skel-	A-Murphy	Bone Tumor Conference	
204—Bromer	etal Changes in Diseases of Children	101—George	Roentgenologist in Industrial Medicine. Roentgenologist	
211—Cole	Pneumoconiosis		as an Expert Witness	
214—Dyke	Pneumo-encephalographic Diagnosis of Brain Tumors	313—Merritt	Technique of Treatment of Cancer of Cervix and Re- sults Therefrom	
221-Macmillan	Roentgen Examination of the	317—Quick		
·	Accessory Nasal Sinuses		Radiation Treatment of Nec Metastasis	
223—Nichols	Diagnosis of Renal Tumors		Dosage Measurement from a	
224—Peirce	Bronchographic Demonstra- tion of Anatomy and Pa-	321—Taft	Clinical Standpoint	
	thology of Bronchial Tree		Radium Dosage	
230—Stewart Huber	Lesions of Lower Esophagus and Cardiac Portion of Stomach	######################################		

	CONDENSED SCHEDULE	OF COURSES OF	N FRIDAY
Code: F-1	1st PERIOD—2:00 to 2:50 Code: F		
•	SL-4Albright	Special Lecture: Ost	reoporosis
Code: F-2	2nd PERIOD	-3:00 to 4:15	Code: F-2
Diagnostic Roentgenology		Therapeutic Radiology	
208—Chamberlain	Technique and Interpretation of Oxygen Myelography	305—Fricke	Radiation Therapy in Carcinoma of the Rectum
210—Codman Blackett	The Shoulder	306—Glasser Portmann	Dosage Measurements with Thimble Chamber: Practi- cal Applications
218—P. C. Hodges	Roentgen Pelvimetry and Fetometry; Orthometric Reproduction	308—Desjardins	Roentgen Treatment of In- flammatory Conditions
219—Kirklin	Stomach and Duodenum after Operation: Roentgenologic Findings	312—Martin	Radiation Treatment of Cancer of Lip and Mouth, including Cervical Metastasis
226—Rigler	Roentgen Diagnosis of Pleural Effusions	313—Merritt	Technique of Treatment of Cancer of Cervix and Re- sults Therefrom
233—Thoma	Diseases and Tumors of the Jaw	314—Newcomet	Radium Therapy of Hem-
Vogt 234—Wyatt	The Heart and Lungs in Children		angiomata

Code: F-3	3rd PERIOD—4:30 to 5:45 Code: F-			
Diagnostic Roentgenology		Therapeutic Radiology		
201—Archer	Roentgen Manifestations in Osteomyelitis	302—Dresser	Roentgen and Radium Therapy	
204—Bromer	Differential Diagnosis of Skeletal Changes in Diseases of	304—Failla	Some Aspects of Radiosen- sitivity	
206—Carty	Children Soft Tissue Roentgenography	310—Lenz	Roentgen Therapy in Cancer of the Larynx and Pharynx	
222—Macmillan	Roentgen Examination of the Mastoids	311—Leucutia	Radiation Therapy in Tu- mors of Bone	
227—Robins	Utero-salpingography	315—Pfahler	Radiation Treatment of Can-	
229—Schatzki	Roentgen Diagnosis of Gas-		cer of the Breast	
229—Schatzki	tritis		Radiation Therapy in Cancer	
232—Swenson	Neoplasms of the Small Intestine		of the Skin	

# AMERICAN RADIUM SOCIETY

The Twenty-fifth Annual Meeting of the American Radium Society will be held in New York City at the Hotel Waldorf Astoria on Monday and Tuesday, June 10 and 11, 1940. The following is the program which has been arranged:

### Program

# Monday, June 10, 1940

Morning Session (Empire Room)

8:30 A.M. Executive Session 9:00 A.M. Scientific Session

- I. Presidential Address. Lawrence A. Pomeroy, M.D., Cleveland, Ohio
- 2. The Need for Clinical Classification of Cancer. Peter A. Nelson, M.D., Chicago, and Herbert E. Schmitz, M.D., Chicago (by invitation).
- 3. Treatment of Large Subcutaneous Hemangiomas with Removable Platinum Implants. Milton Friedman, M.D., New York City.
- 4. The Radium Treatment of Angiomas. Frank E. Simpson, M.D., and J. Ernest Breed, M.D., Chicago.
- 5. Pulmonary Lesions in the Lymphomas. Lloyd F. Craver, M.D., New York City. Discussion: James Ewing, M.D., and Ernst A. Pohle, M.D.

### Intermission, 10 minutes

- 6. The Treatment of Leukoplakia Buccalis and Related Lesions with the Sex Hormones. Ira T. Nathanson, M.D., and David G. Weisberger, M.D., Boston (by invitation).
- 7. Carcinoma of the Penis. Louis H. Jorstad, M D., St. Louis, Missouri (by invitation).
- 8. The Treatment of Cancer of the Rectum. George S. Sharp, M.D., Pasadena, California.

Discussion: C. P. Rhodes, M.D., Archie L. Dean, M.D., and George E. Binkley, M.D.

Monday, June 10, 1940

Afternoon Session (Empire Room)

2:00 P.M. Executive Session 2:20 P.M. Scientific Session

# Chairman, Frederick W. O'Brien, M.D., Boston

- 9. The Treatment of Cervical Metastatic Cancer. Hayes E. Martin, M.D., New York City.
- 10. Complications Following Irradiation of Breast Cancer. Joseph H. Farrow, M.D., New York City (by invitation).
- 11. Irradiation Pulmonary Fibrosis. Bernard P. Widmann, M.D., Philadelphia.

Discussion: Charles L. Martin, M.D., Frank E. Adair, M.D., and Harriet C. McIntosh, M.D.

Intermission, 20 minutes

4:00 P.M. Janeway Lecture

The Specification of Dosage in Radium Therapy. Edith H. Quimby, M.A. Memorial Hospital, New York City.

# Monday Evening, June 10, 1940 Annual Dinner

Hotel Waldorf Astoria—Sert Room Reception and Apéritifs at Seven Dinner at Eight Remarks by the President Presentation of The Janeway Medal to Edith H. Quimby, M.A. Music—Dancing

Tuesday, June 11, 1940 Morning Session (Empire Room)

8:30 A.M. Executive Session 9:00 A.M. Scientific Session

# Chairman, Hayes E. Martin, M.D., New York City

- 12. The Surgery of Post-irradiation Necrosis. Ernest M. Daland, M.D., Boston (by invitation).
- 13. Cancer of the Stomach in the Young. Gordon P. McNeer, M.D., New York City (by invitation).
- 14. Failures in Radiotherapy for Uterine Bleeding and Fibromyomata. James A. Corscaden, M.D., New York City.
- 15. Comments on the Treatment and Sequelae of Carcinoma of the Uterus. Elizabeth Newcomer, M.D., Denver, Colorado (by invitation).

Discussion: Douglas Finch, M.D., George T. Pack, M.D., and Louis E. Phaneuf, M.D.

# Intermission, 10 minutes

16. Carcinoma of the Uterine Cervix Treated with 400 kv. Roentgen Rays and Radium. John T. Murphy, M.D., and C. E. Hufford, M.D., Toledo, Ohio.

 Analysis of 700 Cases of Carcinoma of the Cervix. Harold G. F. Edwards, M.D.,

Shreveport, Louisiana.

18. The Salvage in Vulvar and Cervical Cancer with Lymph Node Metastasis. Fred J. Taussig, M.D., St. Louis, Missouri.

19. Carcinoma of the Cervix Uteri in Childhood and Adolescence. A Review of the Literature and Report of an Additional Case of a Girl Aged Thirteen Years. Harry H. Bowing, M.D., and J. A. L. McCullough, M.D., Rochester, Minnesota.

Discussion: Maurice Lenz, M.D., William P. Healy, M.D., and A. N. Arneson, M.D.

Tuesday, June 11, 1940 Afternoon Session

2:00 P.M. Executive Session 2:20 P.M. Scientific Session

> Chairman, Eugene T. Leddy, M.D., Rochester, Minnesota

- 20. The Progress of Radium since its Earliest Therapeutic Availability. Albert Soiland, M.D., Los Angeles, California.
- 21. Radium Beam Therapy. Ira I. Kaplan, M.D., New York City.
- 22. The Experimental Modification of the Sensitivity of Yeast to Roentgen Rays. Robert S. Anderson, Ph.D., New York City.
- 23. The Influence of Radiation and Hibernation on Growth Behavior of Mouse Neoplasms. Henry J. Ullmann, M.D., Fritz Bishop, and Louisa Long, Santa Barbara, California.

Discussion: Max Cutler, M.D., A. W. Oughterson, M.D., and Fred W. Stewart, M.D.

- 24. Some Considerations Regarding Induced Radioactivity. G. N. Glascoe, New York City (by invitation).
- 25. The Significance of Specific Ionization in the Biological Action of Various Radiations. Raymond E. Zirkle, Bryn Mawr, Pennsylvania (by invitation).
- 26. Protection of Personnel against Wide

Therapy Beams of Roentgen and Gamma Rays. T. R. Folsom and B. Focht, New York City.

Discussion: G. Failla, Edith H. Quimby and Lauriston S. Taylor. Final Adjournment

# BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

The following letter written by Dr. Thomas A. Groover\* to the secretary of the Inter-Society Committee for Radiology is of such universal interest that Dr. Groover's permission to publish it has been secured.

The views of other readers on the topic of hospital relationships will be welcome. The members of the Inter-Society Committee would appreciate receiving comments from members who feel they have something to add to a consideration of the problem. The letter follows:

My dear Cahal:

Many thanks for your letter of December 20th reminding me of a promise to you and Ed Chamberlain to set down some of the thoughts which I expressed at our recent conference in Atlanta regarding the Physician-Hospital relationship problem in which radiologists are particularly interested.

Before attempting to do so first let me say that I think you rightly assume it to be at least part of your function as Executive Secretary of the American College of Radiology to help interpret the specialty to the public and to groups of physicians organized along lines similar to the one you represent. You rightly also regard it as your responsibility to interpret to the medical profession the concepts of the man in the street. To discharge such obligations is a whale of a job. It is one that invites sniping from all sides and requires a superabundance of imperturbability to carry on with it. Probably all of us are opportunists in varying degree and for that reason the gospel of a practical idealism which you are presumed to preach makes yours a most discouraging task. Now, I am about to lay on your doorstep another idea to interpret.

It is chock full of dynamite but I believe it is

\* It is with regret that we announce the death of Dr. Groover, which occurred on April 20, 1940.—Ed.

fundamental to a reasonable understanding of the Physician-Hospital problem.

I think that the problem itself has been in the making for some time but is only just beginning to assume a recognizable form. It is born of the rapid institutionalization of medicine in recent years which still continues at an unabated pace. It should be remembered that the hospital was originally an institution only for the indigent and was commonly an annex of the alms house and prison. Under such circumstances it was natural for the doctor to expect others to furnish the necessary shop, tools and assistants to enable him to function in the hospital, particularly in view of the fact that his own indispensable service was rendered gratuitously. In those days those who were economically competent never thought of patronizing the hospital as patients. Later on when their prejudice against doing so was broken down and they began to patronize hospitals as patients, the hospitals continued to furnish the doctor, without charge to him, a shop in which to work; the tools of his trade; and a corps of professional and technical assistants. Prior to this time the doctor had furnished these items himself in caring for the economically competent. Obviously this circumstance places the doctor in a very vulnerable position with respect to his control of hospital policies. As hospitals continue to occupy an increasingly dominant position in the medical field, concurrently with an increasing institutionalization of medicine, the doctors' influence in controlling their policies may reasonably be expected to dwindle proportionately. As a corollary of the latter statement it is logical to conclude that the "fee for service" system of medical practice will decrease, and the "wage for service" system will increase. I think that this trend is now apparent in many departments of medicine—obviously so in radiology—and I believe that many adherents of the fee for service system in all departments of medicine will be drawn into the opposing group and still larger numbers will quite naturally grow up in it.

To state the problem in a somewhat different way I envision the hospitals as representing the capitalists of medicine, and would regard it as passing strange if they do not more and more adopt the capitalistic technique. By the latter

I mean more particularly that increasing pressure will be exerted to hire professional help just as they do nonprofessional. Certainly the present differential in the doctor's favor will in one way or another be wiped out.

Assuming now that a large segment of the medical profession recognizes and views adversely the trend I have tried to indicate, it may well be asked what, if anything, can they do to modify it. To such I would have them remember that it is their prerogative to operate their own shop. In other words they can form a competing capitalistic group. There is abundant evidence to indicate that this is not an altogether fantastic idea or impractical task. If undertaken seriously it may well have a far reaching and salutary effect both for the medical profession and the public.

In the above brief commentary on the Physician-Hospital problem I trust that you will particularly note that it is not tinged with partisanship or special pleading. I have purposely refrained from even mentioning many highly important issues and implications which the basic theme suggests, feeling that to do so might obscure rather than clarify the latter. I would be glad to discuss some of the former with you when the opportunity offers.

Sincerely yours, (Signed) Thos. A. Groover

# KENTUCKY RADIOLOGICAL SOCIETY

The Annual Meeting of the Kentucky Radiological Society was held at the Brown Hotel, Louisville, Kentucky on Sunday, April 21, 1940. The meeting convened at 11:20 A.M. with Dr. D. B. Harding, President, presiding. Following the business session luncheon was served. After the luncheon Dr. Howard P. Doub, of Detroit, Michigan, addressed the Society on the subject of "Childhood Tuberculosis." His presentation was illustrated by numerous lantern slides. Following Dr. Doub's address cases illustrated by lantern slides were reported by members of the Society and were discussed by those present. The meeting adjourned at 5:30 P.M.

# BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

ROENTGEN DIAGNOSIS OF THE EXTREMITIES AND SPINE. (Ann. Roentgenol., Vol. XVII.) By Albert B. Ferguson, M.D., Director of Roentgenology, New York Orthopaedic Hospital; Instructor in Orthopaedic Surgery, College of Physicians and Surgeons, Columbia University. Cloth. Price, \$12.00. Pp. 435, with 513 illustrations. New York: Paul B. Hoeber, Inc., 1939.

This latest addition to the Annals of Roentgenology presents the subject of skeletal roentgenology in the precise, organized fashion so characteristic of this author's teaching methods. The book is addressed to the medical profession at large and therefore attempts to justify the roentgenologic manifestations of skeletal disease on the basis of purely objective evidence which can be appreciated and understood by any careful observer.

No attempt has been made to treat separate disease entities exhaustively from all points of view; instead the text deals in an extremely orderly fashion with various appearances of bone and cartilage in health and disease. The introduction sets the pace of the entire volume by introducing the highly definitive roentgenologic nomenclature developed and employed by the author which is rigidly followed throughout the text. The reader may find in this lexicon of terms many which are not in common and widely accepted usage. He may disagree with the author's belief that neoplasia, lues, and nonspecific inflammatory disease, for example, produce individually characteristic degrees of bone density which can be recognized as such by the roentgenologist with any considerable degree of accuracy. It must be admitted, however, that the specific terminology employed is preferable to haphazard, wordy description. Never are descriptive terms used loosely or ambiguously; definitions provided at the outset are never violated.

This book is not one to be read lightly, for both in the matter of content and arrangement it requires the full and undivided attention of the reader. The specialized roentgenographic nomenclature mentioned above appears, wherever it occurs, in bold face type to arrest one's attention. Illustrative material is so profuse that repeated interruptions of continuity in the text are unavoidable, and clinical information about each case whose roentgenograms have been reproduced is cataloged at the end of each chapter and rendered accessible by means of reference numerals. These numerous annotations prevent brisk, casual reading.

Both the author and the publisher are to be complimented on the general excellence of this book. Because so many illustrations have been employed, it has obviously been necessary to limit the size of individual cuts which renders it somewhat difficult to quickly recognize the exact location of bones illustrated. For those who prefer to observe roentgenograms in the form of original negatives, these printed positives require mental transposition. Here again, however, uniformity and consistency have been the rule and in general the reproductions are of excellent quality. Virtually every phase of skeletal roentgenology has been richly and advantageously illustrated. Practitioners and students alike will find in Ferguson's contribution an excellent reference work.

Fred Jenner Hodges

CANCER HANDBOOK OF THE TUMOR CLINIC, STANFORD UNIVERSITY SCHOOL OF MEDICINE. Edited by Eric Liljencrantz, M.D., Chief of Tumor Clinic, Stanford University School of Medicine; Consultant in Neoplastic Disease, United States Naval Hospital, Mare Island, and United States Marine Hospital, San Francisco. Cloth. Price, \$3.00. Pp. 114, with 50 illustrations. Stanford University, California: Stanford University Press, 1939.

This book is a revision of the syllabus on the diagnosis and treatment of malignant tumors originally published at the Stanford University School of Medicine in 1937. It presents the methods of diagnosis and treatment of malignant neoplasms currently in use in the Tumor Clinic of that institution. The first twenty-four pages deal with general considerations, and here the up-to-date character of its summaries is evidenced by the inclusion of extra-chromosomal factors among the intrinsic causes of cancer, by brief discussion of the more im-

portant chemical carcinogens and by reference to the new-growths known to be induced by viruses. It is stated emphatically that whatever the theoretical dangers of biopsy may be, far more serious are the dangers of attempting radical treatment or of declaring the prognosis hopeless without tissue proof. Properly performed biopsy is less dangerous than is rough handling or massage by patient or physician. The principles of radiation therapy receive proportionally fuller exposition than do the other topics in this section and the Amstutz diagram illustrating the range and relationship of electromagnetic waves is reproduced. Chapters on cancer of the skin, eve and lip, oropharvnx and neck, gastrointestinal tract, lung, breast, female generative tract, genitourinary tract, on leukemias and lymphoblastomas, on tumors of the central nervous system and on bone tumors follow. A bibliography with selected references arranged by chapter headings and a complete index are provided. For each common form of malignant disease there is a brief discussion of methods of diagnosis and of treatment. Naturally enough, not every reader will be in full accord with all of the methods of treatment advised, for there is still considerable diversity of opinion among competent authorities. Yet the methods given are those which have proved to be most useful in a cancer clinic in which the combined judgment of a group of specialists is utilized. As such, these recommendations must receive thoughtful consideration. Moreover, they represent very fully the prevailing methods in other active cancer clinics. This book will prove very useful to the postgraduate student in the field of neoplasia and to the general practitioner. Upon the latter it places the chief responsibility for the fate of the cancerous patient. C. V. Weller

Tumors of the Skin, Benign and Malignant. By Joseph Jordan Eller, M.D., Attending Dermatologist, City Hospital, New York City; Consulting Dermatologist, French Hospital and Broad Street Hospital, New York City; Unity Hospital, Brooklyn; Morristown Memorial Hospital, Monmouth Memorial Hospital, Norwalk General Hospital, etc. Cloth. Price, \$10.00. Pp. 607, with 401 illustrations. Philadelphia: Lea & Febiger, 1939.

Concise descriptions of the many tumors found in the skin illustrated with many good

photographs and photomicrographs are presented in this volume. Histological studies of the relatively unimportant benign tumors included in the first section of the book are particularly valuable because they are not found in most texts. In a chapter entitled, "Nevi and Other Developmental Disturbances of the Skin," an attempt is made to unscramble a large group of poorly understood conditions known by a variety of names which are rather mystifying to the uninitiated.

A discussion of the etiology of tumors seems rather inadequate since no mention is made of the voluminous work recently published dealing with the carcinogenic properties of coal-tar derivatives and estrogenic substances.

Precancerous lesions are described in some detail and 250 pages are devoted to malignant new growths, including malignant melanomas, sarcomas, lymphomas and carcinomas peculiar to the epithelium covering the various portions of the body and its orifices. The author should be highly commended for the chapter on therapy because, so far as the reviewer is aware, he is the first American dermatologist to boldly advocate adequate doses of radiation for cancer of the skin since Pusey published his original book about thirty years ago. The treatment of a number of actual cases is illustrated with charts and in most instances efficient plans for treating the lesions with roentgen rays, radium, coagulation, or surgery are outlined. The proper use of only one method is advocated in each instance, rather than the old dermatological practice of combining several procedures in a half-hearted manner.

Although the care of small carcinomas is well covered, a section dealing with the use of high voltage roentgen rays and interstitial radium sources in the treatment of large carcinomas and metastatic lymph nodes should be added to the next edition. A statistical study of the results obtained with different methods in the author's large material would also be of great interest.

For the sake of completeness a chapter on the simple principles of cutaneous surgery and plastic repair is included and a short appendix contains practical and reliable data on radiation physics and dosage. The bibliography is ample, and the cooperation of a series of outstanding pathologists, surgeons, radiologists and dermatologists accounts for the unusual comprehensiveness of this very excellent book.

CHARLES L. MARTIN

THE COMPARATIVE VALUES OF CHEST ROENT-GENOGRAMS MADE ON FILM AND ON PAPER FOR INDUSTRIAL SURVEYS. By Air Hygiene Foundation of America, Inc. Medical Series, Bulletin No. 11. Paper. Price, \$2.00. Pp. 20, with charts and illustrations. Pittsburgh, Pa., 1939.

In 1938, the Air Hygiene Foundation requested the University of Pennsylvania to make a study of available roentgenologic methods for examination of the chest of large groups of employees with special reference to the primary importance of diagnostic accuracy, of time consumed in such examinations and cost involved in the equipment and photographic medium used. The study was directed by Dr. E. P. Pendergrass of the Department of Radiology of the Hospital of the University of Pennsylvania and technical aspects were developed by the staff of the Moore School X-ray Laboratory comprising Professor Charles Weyl, Dr. S. Reid Warren, Jr., and Mr. Dallett B. O'Neill. Forty-nine roentgenologists examined test roentgenograms and recorded their opinions in special questionnaires.

Two methods of examination were studied from the standpoints mentioned above: (1) the use of 14×17 inch roentgen film, and (2) the use of sensitized paper. The object of the study was to attempt to answer the question, "What are the comparative values of single roentgenograms on film and paper?"

The report consists of twenty pages and six large charts with several additional tables within the text. The material is divided into the following sections:

(1) The physical characteristics of roentgenograms on film and paper. (2) Preliminary experimental procedures. (3) Roentgenographic exposure techniques. (4) Test roentgenograms and questionnaires. (5) Physical data of test roentgenograms. (6) Roentgenologists' comments on test roentgenograms. (7) Conclusions.

Condenser discharge apparatus was used for both film and paper exposures. Comments of the roentgenologists who examined the roentgenograms are given in considerable detail and the description of the preliminary experimental procedures and techniques employed indicates painstaking effort to arrive at correct conclusions.

The authors conclude that their results demonstrate two points:

1. The paper roentgenograms produced in

the tests were of better quality than those produced by other methods heretofore used in survey work.

2. Many roentgenologists learn easily and quickly the technique of viewing paper roentgenograms even though they may formerly have been unfamiliar with the use of this roentgenographic medium.

They admit that some time will be required to set up methods whereby paper roentgenograms may be routinely made in accordance with the technical procedures described in their report. They believe, however, that it is possible to devise and put into effect such technical methods ultimately as routine procedures. In view of the fact that no evidence was produced in their study to show that paper roentgenograms are in any way superior to those on film from the diagnostic standpoint, they feel it is best in the long run to devise a method of making roentgenograms on film quickly and at low cost. If a large group of employees is to be examined and a part of the examination is a single roentgenogram of each employee, then it is less expensive and less time-consuming to use paper in rolls than to use single pieces of film. Such a survey may be made with paper if the technical methods outlined in their report are used or if other methods are used which produce equal or better results.

This report is well worth careful consideration by all roentgenologists. For those whose practice includes surveys of industrial plants, schools, colleges, etc., it is an indispensable addition to their book shelves.

R. S. Bromer

A Textbook of Surgery. By John Homans, M.D., Clinical Professor of Surgery. Compiled from lectures and other writings of members of the Surgical Department of the Harvard Medical School. Fifth Edition. Cloth. Price, \$8.00. Pp. 1272, with 530 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

The fifth edition of this popular textbook of surgery has been extensively revised, if that is the term, with the complete replacement of outworn observations and procedures by the newer discoveries and advances in surgery. Every section of the book has been subjected to this process and there is included now in this edition the surgical advances that have occurred since the printing of the fourth edition. The pagination has remained unchanged and con-

sequently the book remains the same size, the new sections having replaced outworn items. It is in essence a rewriting of the work so that it retains its freshness and the charming personal style of the author. This edition, like the others, is an excellent example of the printer's and book-binder's art and it can be highly recommended to the student of surgery, especially to the one in medical school, as the book is after all written for him, and still continues to fulfill this function admirably.

FREDERICK A. COLLER

### BOOKS RECEIVED

A TEXT-BOOK OF X-RAY DIAGNOSIS. By British Authors. In three volumes. Volume III. Edited by S. Cochrane Shanks, M.D., M.R.C.P., F.F.R., Honorary Director, X-Ray Diagnostic Department, University College Hospital; Radiologist, the Prince of Wales's General Hospital, etc., Peter Kerley, M.D., M.R.C.P., F.F.R., D.M.R.E., Physician to the X-Ray Department, Westminster Hospital; Radiologist, Royal Chest Hospital, etc., and E. W. Twining, M.R.C.S., M.R.C.P., F.F.R., D.M.R.E., Radiologist, Royal Infirmary, Manchester; Radiologist, Christie Hospital; Later Hunterian Professor, Royal College of Surgeons; Lecturer in Radiology, University of Manchester, etc. Cloth. Price, £3.3.0. Pp. 800, with 710 illustrations. London: H. K. Lewis & Co., Ltd., 1939.

THE 1939 YEAR BOOK OF RADIOLOGY. Diagnosis: Edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University; Assistant Visiting Roentgenologist, Johns Hopkins Hospital, and Whitmer B. Firor, M.D., Associate Editor, Assistant in Roentgenology, Johns Hopkins University; Assistant in Roentgenology, Johns Hopkins Hospital. Therapeutics: Edited by Ira I. Kaplan, B.Sc., M.D., Director, Division of Cancer, Department of Hospitals, City of New York; Clinical Professor of Surgery, New York University Medical College; Director, Radiation Therapy Department, Bellevue Hospital, New York City, etc. Cloth. Price, \$4.50. Pp. 528, with 509 illustrations. Chicago: The Year Book Publishers, Inc., 1939.

THE HOSPITAL CARE OF NEUROSURGICAL PATIENTS. By Wallace B. Hamby, M.D., F.A.-C.S., Associate Professor of Neurology and

Instructor in Surgery (Neurological Surgery), University of Buffalo School of Medicine, Buffalo. Cloth. Price, \$2.00. Pp. 118. Springfield, Illinois: Charles C Thomas, 1940.

THE HYPOTHALAMUS AND CENTRAL LEVELS OF AUTONOMIC FUNCTION. Proceedings of the Association December 20 and 21, 1939, New York. (Research Publications, Association for Research in Nervous and Mental Disease, Vol. XX.) Editorial Board: John F. Fulton, M.D., Chairman, S. Walter Ranson, M.D., and Angus M. Frantz, M.D. Cloth. Price, \$10.00. Pp. 980, with 319 illustrations and 35 tables. Baltimore: Williams & Wilkins Co., 1940.

L'ÉLECTRO ENCÉPHALOGRAMME: NORMAL ET PATHOLOGIQUE. Par Ivan Bertrand, Directeur à l'École des Hautes Etudes, Jean Delay, Médecin des Hôpitaux de Paris, and Jacqueline Guillain, Assistante à l'Institut de Neurobiologie. Paper. Price, 94 fr. Pp. 294, with 94 illustrations. Paris: Masson et Cie, 1939.

TRAUMI CRANICI: CHIRURGIA—NEUROLOGIA—RADIOLOGIA. By Mario Lapidari, Ludovico Mucchi, and Virginio Porta. Con un capitolo sulla lesioni auricolari da trauma cranico di F. Carnevale Ricci. Prefazione de Mario Donati. Paper. Price, 50 lire. Pp. 430, with 101 illustrations. Belluno: Edizioni Casa Editrice Libraria Antonio Salvador, 1938.

ELECTROCARDIOGRAPHIC PATTERNS: THEIR DIAGNOSTIC AND CLINICAL SIGNIFICANCE. By Arlie R. Barnes, M.D., Mayo Clinic, Rochester, Minnesota. Cloth. Price, \$5.00. Pp. 197, with 95 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

Peripheral Vascular Diseases: Diagnosis and Treatment. By William S. Collens, B.S., M.D., Metabolist, Chief of the Clinic for Peripheral Vascular Disease, Chief of the Diabetic Clinic, Israel Zion Hospital, Brooklyn, etc., and Nathan D. Wilensky, M.D., Assistant in Clinic for Peripheral Vascular Disease, Assistant in Diabetic Clinic, Israel Zion Hospital, etc. Cloth. Price, \$4.50. Pp. 243, with 77 illustrations. Springfield, Illinois: Charles C Thomas, 1939.

THE ELECTROCARDIOGRAM AND X-RAY CONFIGURATION OF THE HEART. By Arthur M. Master, B. S., M.D., F.A.C.P., Associate in

Medicine and Chief, Cardiographic Laboratory, the Mt. Sinai Hospital, New York: Associate in Medicine, the College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, \$6.50. Pp. 222, with 71 illustrations. Philadelphia: Lea & Febiger, 1939.

THE DIAGNOSIS AND TREATMENT OF DISEASES OF THE ESOPHAGUS. By Porter P. Vinson, B.S., M.A., M.D., D.Sc., F.A.C.P., Professor of Bronchoscopy, Esophagoscopy, and Gastroscopy, Medical College of Virginia, Richmond, Virginia. Cloth. Price, \$4.00. Pp. 224, with 98 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

THE INTRODUCTION OF GASTRO-ENTEROLOGY. Third Edition of The Mechanics of the Digestive Tract. By Walter C. Alvarez, Professor of Medicine, University of Minnesota, The Mayo Foundation, and a Senior Consultant in the Division of Medicine, The Mayo Clinic. Cloth. Price, \$10.00. Pp. 778, with 186 illustrations. New York: Paul B. Hoeber, Inc., 1940.

PROCTOSCOPIC EXAMINATION AND DIAGNOSIS AND TREATMENT OF DIARRHEAS, By M. H. Streicher, M.S., M.D., Assistant Professor of Medicine, University of Illinois, College of Medicine, Research and Educational Hospital, and Department of Surgery, Grant Hospital of Chicago. Cloth. Price, \$3.00. Pp. 139, with 39 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

ORTHOPEDIC OPERATIONS: INDICATIONS, TECH-NIQUE AND END RESULTS. By Arthur Steindler, M.D., F.A.C.S., Professor of Orthopedic Surgery, The State University of Iowa, Iowa City, Iowa. Cloth. Price, \$9.00. Pp. 766, with 322 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

ENDOCRINE GYNECOLOGY. By E. C. Hamblen, B.S., M.D., F.A.C.S., Associate Professor of Obstetrics and Gynecology, Duke University School of Medicine; Gynecologist in charge of the Endocrine Division and Sex-Endocrine Clinic, Duke University Hospital. Durham, North Carolina. Foreword by J. B. Collip, M.D., Gilman Cheney Professor of Biochemistry and Pathological Chemistry, McGill University, Montreal. Cloth. Price, \$5.50. Pp. 453, with 169 illustrations. Springfield, Illinois: Charles C Thomas, 1939.

HANDBOOK OF THE HOSPITAL CORPS, UNITED STATES NAVY, 1939. Published by the Bureau of Medicine and Surgery, under the Authority of the Secretary of the Navy. Cloth. Price, \$1.75. Pp. 1015, with 201 illustrations. Washington, D. C.: U. S. Government Printing Office, 1939.

Ergebnisse der Gesamten Tuberkulosefor-SCHUNG. Band IX. Herausgegeben von H. Assmann, Königsberg I. Pr.; H. Beitzke, Graz; and H. Braeuning, Hohenkrug-Stettin. Paper, Price, RM. 56; bound, RM. 58. Pp. 577, with 135 illustrations. Leipzig: Georg Thieme, 1939.

Das Wesen und der Wert der Tomographie (Praktische Tuberkulose-Bücherei, Heft 23.) Von Dr. W. Deutschmann, Aus den Heilstätten der L.V.A. Berlin, Ärztlicher Direktor: Dr. Kremer. Paper. Price, RM. 3. Pp. 40, with 39 illustrations. Leipzig: Georg Thieme, 1939.

Grundlagen der Röntgendiagnostik und RÖNTGENTHERAPIE. Von Chefarzt Dr. G. Schulte, Knappschafts-Krankenhaus Recklinghausen, und Doz. Dr. med. habil. F. Kuhlmann, Medizinische Universitätsklinik Halle a. S. Paper, price, RM. 7.50; bound, RM. 8.50. Pp. 140, with 148 illustrations. Leipzig: Georg Thieme, 1939.

Ergebnisse der Physikalisch-diätetischen THERAPIE. Ingemeinschaft mit Prof. Dr. W. Heupke, Oberarzt an der Med. Universitäts-Poliklinik Frankfurt a. M., Hofrat Dr. J. Kowarschik, Primärarzt und Vorstand des Institutes für physikalische Heilmethoden im Krankenhaus der Stadt Wien, and Doz. Dr. J. Kühnau, Direktor des Städt. Forsch.-Inst. für Bäderkunde und Rheumaheilanst Wiesbaden. Herausgegeben von Prof. Dr. H. Lampert, Direktor des Univ.-Inst. für physikalische Therapie, Frankfurt a. M., und des Univ.-Inst. für Quellenforsch und Bäderlehre, Chefarzt am Kreiskrankenhaus Bad Homburg v.d.H. Band 1. Paper, price, RM. 25.50; bound, RM. 27. Pp. 410, with 94 illustrations. Dresden and Leipzig: Theodor Steinkopff, 1939.

Handschrift und Eigenart der Krebsge-FÄHRDETEN: Ein Beitrag zur Dispositionsforschung. By Etel Vértesi. Cloth. Price, \$4.00. Pp. 297, with 130 illustrations of handwriting. Budapest: Brüder Tisza, 1939.

# DEPARTMENT OF TECHNIQUE

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# A METHOD FOR THE PREPARATION OF RADON OINTMENT

By LESTER J. PERLMAN chicago, Illinois

IN A RECENTLY published paper Uhlmann has again called attention to the value of radon ointment in the treatment of irradiation injuries. Eidinow has de-

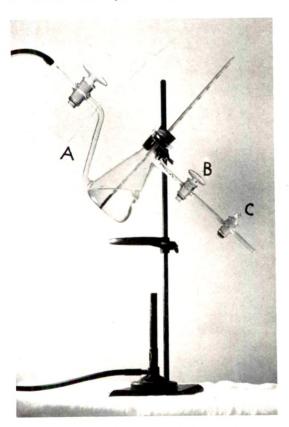


FIG. 1. The apparatus tilted for evacuation; the water bath is removed to show the vaseline level.

scribed its use in other skin conditions. Radon ointment is a physical mixture or solution of a minute quantity of gaseous radon in vaseline. Ashort time after its preparation, this mixture also contains small

but important equilibrium quantities of the radioactive decay products of radon. The method given below was devised for the routine preparation of such a radon ointment.

The radon used is the "residual fraction" obtained in the preparation of radon implants after the method of Failla and Duane. It is contained at  $\frac{1}{3}$  to  $\frac{1}{2}$  atmospheric pressure in glass capillary tubes less than 1 mm. in diameter and 20 to 50 mm.

The apparatus used is shown in Figure 1 and is constructed of an ordinary heavywalled "Pyrex" filter flask with an additional sidearm (A) sealed at the bottom angle of the flask and curving upward. The upper sidearm (B-C) bears in series two "Pyrex" stopcocks (B) and (C) of 2 mm. bore, while the other sidearm (A) carries one stopcock (A) of 4 mm. bore. Two sets of apparatus are used, one of 125 cc. capacity for the preparation of 2 oz. (60 cc.) of ointment, and one of 250 cc. capacity, for the preparation of 4 oz. of ointment. In use the flask is supported in a hot water bath (not shown in the figure) on a ringstand by means of a burette clamp having a universal joint.

With stopcocks (B) and (C) in the open position the radon tube is placed in sidearm (B-C) and with a thin applicator stick is moved into position within the bore of stopcock (B). A trace of stopcock grease serves to maintain this position during subsequent manipulation of the apparatus. Stopcock (C) is then closed.

The vaseline, melted in its original con-

tainer in the water bath, is poured into the flask, and the flask is sealed with a oneholed rubber stopper bearing a thermometer. The apparatus is then tilted until sidearm (A) is brought above the level of the liquid vaseline, and the flask is lowered into the water bath, leaving the stopcocks above the water. A rubber tube from a vacuum pump is connected to the sidearm (A), and, with the water bath at close to boiling, the flask is slowly evacuated through stopcock (A), until the frothing of the vaseline is in large measure ended. The vacuum so obtained later facilitates the rapid diffusion of the radon through the apparatus. Stopcock (A) is closed, the rubber tubing removed, and the flask returned to upright position in the water bath.

Now stopcock (B) is turned through 180°, breaking the radon tube and permitting the radon to diffuse into the flask. The burner is removed from under the water bath, and the burette clamp is disconnected from the ringstand. A rotary motion of the flask, still in the water bath, imparts a swirling agitation to the vaseline, speeding the dissolving of the radon. The whole is permitted to cool slowly with intermittent agitation for about twenty minutes, until the thermometer reads 50–55° C. (The vaseline will not flow readily below about 50° C.)

Stopcock (C) is gently opened, admitting air to the flask, the apparatus is removed from the water bath, and the vaseline is poured through sidearm (A) into a screw-capped jar which is immediately capped tightly. Care must be taken to close stopcocks (A) and (C) before all the vaseline has drained from sidearm (A). This traps most of the undissolved radon in the flask.

Measurements with a gamma-ray elec-

troscope indicate a yield of about 65 per cent of the original radon in the ointment. Measurements of unopened jars of ointment on successive days show a decrease of activity in accordance with the rate of decay of the radon (about half-destroyed every four days) and give no evidence of loss from closed jars by leakage or "evaporation." Thus the preparation and measurement of the ointment some days before use is feasible.

The method gives consistent results over a wide range of radon concentrations. It has also been applied to the preparation of beeswax beta-ray plaques of low intensity such as those used in dermatology by Lomholt, and its use may be extended to the preparation of radon solutions in other media. The yield may be expected to vary with the solvent and with the temperature at which the process is completed.

This method is alternative to other methods for the production of radioactive vaseline which have been published. References to some of these methods are given.

# REFERENCES

- 1. EIDINOW, A. Radio-active vaseline; a new technique for surface radium therapy. *Practitioner*, 1937, 138, 769-773.
- HAPPEL, P. Die Radiumemanations- Salbentherapie. Deutsche med. Wchnschr., 1934, 60, 1274–1278.
- 3. LOMHOLT, S. Alpha and beta ray therapy in dermatology. Brit. J. Dermat., 1936, 48, 567-582.
- 4. Strasburger, J. Verbesserte Ausnutzung der Radiumemanation durch Bindung an Fett. Deutsche med. W.chnschr., 1923, 49, 1459–1463.
- TSCHELNITZ, H. Über die Bindung der Radiumemanation an fette Absorbentien bei Zusatz von aktiver Kohle. Strahlentherapie, 1937, 59, 157–167.
- UHLMANN, E. The treatment of injuries produced by roentgen rays and radioactive substances. Am. J. ROENTGENOL. & RAD. THERAPY, 1939, 41, 80-90.



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# ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

# ROENTGEN DIAGNOSIS

ABDOMEN

CHAMBERLIN, GEORGE W. The roentgen anatomy of the small intestine. J. Am. M. Ass., Oct. 21, 1939, 113, 1537–1541.

Roentgenologically, the small intestine is a highly active and dynamic organ with certain characteristic anatomic and physiologic features. The meal that the author has used is made of 5 ounces of distilled water and 5 ounces of barium sulfate. Water is distilled to remove the chlorine, which may produce a disturbance in the roentgen appearance of the intestinal tract. In normal controls, the head of the meal reaches the cecum in from one and a half to three hours. The small intestine is completely empty in from five to six hours. The mucosal pattern of the small intestine shows many variations which seem to be specific for a given set of physical conditions. Such a pattern is derived from the primary circular folds of Kerkring and from the secondary induced folds which may occur in the mucous membrane. The pattern of a given segment depends on its anatomic character and also on its physiologic activity at the time of the examination. Intraabdominal hernia can be diagnosed by roentgen study of the small intestine. In this condition the coils are grouped closely and they may occupy the right, left or midabdominal position. Congenital diverticula of the small intestine occur most frequently in the duodenum. Congenital membranes and veils attached to the duodenum may produce roentgenologic appearances which cannot be differentiated from pericholecystic adhesions or duodenal ulcers. Congenital defects which result in a narrowed small intestinal lumen or complete atresia are most commonly found in children. In most of the cases, these defects are incompatible with life. Meckel's diverticulum may sometimes be found. Whenever delayed motility occurs in the ileum, one should examine the intestine carefully for this anomaly. Ileal stasis may result from a Lane's kink. One may suspect this condition if a partial obstruction is associated with a kinked and somewhat fixed terminal ileum.-S. G. Henderson.

Weber, Harry M. Roentgenologic manifestations of non-neoplastic lesions of the small intestine. J. Am. M. Ass., Oct. 21, 1939, 113, 1541–1546.

Peptic ulcer of the duodenum and of the jejunum occurring after gastroenterostomy is omitted. Acute inflammatory processes of the small intestine are not included because patients afflicted with them rarely are, and probably never should be, submitted to roentgenologic examination. Syphilitic and actinomycotic lesions of the small intestine are exceedingly rare. The technique used in examining the small intestine is described.

Tuberculous enteritis and a nonspecific form of chronic enteritis of undetermined origin are the most common types of chronic enteritis encountered in practice. The two diseases have many clinical, morphologic and roentgenologic features in common. Usually in tuberculous enteritis a combination of ulceration and hyperplasia is observed. As a rule, tuberculous lesions are distributed throughout the colon and in the small intestine as well, and especially in the ileocecal region, but there are many exceptions. In 1932 Crohn, Ginzburg and Oppenheimer reported a series of cases of benign, subacute or chronic, necrotizing and cicatrizing inflammation of the small intestine. Macroscopically, it is always difficult, and usually impossible, to distinguish the non-tuberculous from the tuberculous form. Close comparison of the roentgenologic appearances often shows a different roentgenologic "look" of the two diseases. The contours of the tuberculous intestine have typically a rougher, more corrugated appearance corresponding to a more irregular, disconnected insemination of the ulcerohyperplastic process. In the non-tuberculous form of chronic enteritis the contours are characteristically smooth and the narrowing is uniform, corresponding to the typical diffuse, even development of the underlying pathologic process. Other aids in the differentiation are chiefly those concerned with the exclusion of tuberculosis.

Peculiar changes in the roentgenologic appearance of the small intestine are often observed in certain states of dietary deficiency, especially when steatorrhea, with or without

diarrhea, is one of the principal clinical features. One of the surprising features is the marked depression of motility throughout the intestinal tract. Peculiar segmentation of the intestinal loops is commonly found. Contracted segments are observed to alternate irregularly with dilated ones. The contours of well distended segments may be abnormally smooth at one period of roentgenoscopic observation, abnormally shaggy at another. Fantastic agglomerations of the opaque suspension take place. The author believes that the roentgenologic changes are plausibly explained by holding the degenerative changes accountable for the abnormal motility and for some of the bizarre intestinal patterns observed, while abnormal secretions are made responsible for the other peculiar roentgenologic manifestations.

Diverticula are found in the duodenum more frequently than in any other part of the intestine except the sigmoid colon. The most common site of origin is near the ampulla of Vater. The diverticula found in the jejunum are larger, as a rule, than those in the duodenum, and they are more frequently multiple than single. Diverticula are but rarely found in the ileum, and those not designated as Meckel's diverticula rarely are associated with clinical symptoms. Meckel's diverticulum occurs in about 2 per cent of the population, males predominating in a ratio of 2:1. It is always found somewhere in the first 5 feet (150 cm.) of ileum above the ileocecal valve. Only 8 of 20 patients reviewed by Pemberton and Stalker had symptoms believed to be due to the diverticulum. Up to the present time Meckel's diverticula have been demonstrated roentgenologically on but 6 occasions at the Mayo Clinic. Meckel's diverticulum will usually be found in those coils of the lower part of the ileum that are situated near and somewhat to the right of the midline and at or near the level of the umbilicus.

Of the extra-enteral non-neoplastic processes which extend to and involve the small intestine, perforating diverticulitis of the sigmoid colon and salpingo-oöphoritis seem to be encountered most frequently. If actual perforation into the intestinal lumen has not taken place, considerable deformity of the affected segment may be observed, yet as the mucosal surface is carefully examined it will be noted that the mucosal pattern, although altered considerably by functional changes and by edema and submucous infiltration, will be left unbroken throughout the deformed segment.—S. G. Henderson.

KIEFER, EVERETT D. Clinical aspects of chronic disorders of the small intestine. J. Am. M. Ass., Oct. 21, 1939, 113, 1546–1552.

There are few symptoms which are highly diagnostic of disease of the small intestine. The almost completely fluid nature of the content of the small intestine makes for an "all or none" type of obstruction. Abdominal distress immediately after meals, flatulence and diarrhea are suggestive of hypermotility. Grossly inadequate absorption results in large, foul, fatty stools, failing nutrition, calcium imbalance and avitaminosis.

The general physical signs of disease of the small intestine are malnutrition, anemia and signs of vitamin deficiency. An important abdominal finding may be a mass.

By far the most important single laboratory procedure is the roentgen examination of the gastrointestinal tract, but lesions of the small intestine are not found unless they are looked for. A film taken between two and three hours after the barium meal has much more diagnostic value than the ordinary six hour film.

One of the commonest forms of chronic organic disorders of the small intestine is the intermittent obstruction caused by postoperative adhesions. Characteristically the physical examination and the gastrointestinal roentgen films may be entirely negative during the intervals between attacks. Due to fear of eating because of the resulting pain, frequent vomiting and diarrhea, mild states of malnutrition and vitamin deficiency are common, and occasionally avitaminosis develops comparable to severe pellagra.

An annular carcinoma of the small intestine characteristically tends to give rise to slowly progressive obstruction with increasing pain, vomiting and loss of weight. New growths which are mural or polypoid in type are the most frequent cause of intussusception in the adult and are prone to cause intermittent attacks of obstruction. Meckel's diverticulum is another important cause of intussusception in young adults. In cases of bleeding from the lower portion of the intestine, particularly in children and young adults, Meckel's diverticulum should be considered, since the occurrence of aberrant gastric mucosa within the sac giving rise to peptic ulceration, hemorrhage and perforation is a well known clinical entity.

A subacute or chronic non-ulcerative inflammation of the small intestine is frequently seen.

From a roentgenologic point of view, chronic ulcerative enteritis of either the small or the large bowel produces obliteration of normal outlines, loss of flexibility, shortening of loops, stenosis and contraction of the lumen and occasional fistula formation. Tuberculous enterocolitis produces changes in the ileum and proximal colon which, from a roentgenologic standpoint, are indistinguishable from nonspecific enteritis. Hyperirritability of the intestine is indicative of early ulcerative lesions in the mucosa.

Avitaminosis may lead to secondary changes in the intestinal tract which are sufficiently definite to be demonstrated by roentgen study. Irregular distortions of the normal mucosal pattern, localized dilatation of the lumen and a tendency for the barium sulfate to form pockets in isolated loops are noted. Purely functional disorders of the small intestine are usually manifested by signs and symptoms of hypermotility.—S. G. Henderson.

WINTERS, WILLIAM L., and EGAN, SHERMAN. Incidence of hemorrhage occurring with perforation in peptic ulcer. J. Am. M. Ass., Dec. 16, 1939, 113, 2199–2204.

Authors' Summary and Conclusions. Three hundred and sixty-one patients with perforated peptic ulcer that entered Cook County Hospital during the years 1935-1938 inclusive were reviewed to note the incidence of hemorrhage. Bleeding and perforation in a peptic ulcer do occur together. For the four years reviewed, bleeding was present in 10 per cent of the patients with perforated ulcer, and bleeding and perforation occurred in approximately I per cent of all patients admitted with the diagnosis of peptic ulcer during the years 1937 and 1938. Approximately 60 cc. or more of blood has escaped into the bowel when a patient has melena. Perforation in peptic ulcers occurred more often in males than in females. It occurred most frequently in the fourth decade, although the fifth decade showed almost the same number of cases. Bleeding and perforation occurred most frequently together in the sixth decade. Hemorrhage that follows surgical repair of a perforation should arouse suspicion that an ulcer situated elsewhere in the gastrointestinal tract may be responsible for the bleeding.—S.G. Henderson.

Stone, Harvey B., and McLanahan, Samuel. Surgical aspects of carcinoma of the large bowel. J. Am. M. Ass., Dec. 23, 1939, 113, 2282–2288.

In the presence of demonstrable visceral or peritoneal metastases it is often justifiable, and indeed good judgment, to remove an operable obstructing lesion. In a number of cases before ascertaining the operability of a given tumor it is necessary to make a careful, discreet beginning of resection. For the inoperable low sigmoid or rectal growth which at the time of exploration is not obstructing, a knuckle of sigmoid proximal to the growth is brought out through a short left McBurney incision and sutured to the skin. The second stage can be performed when necessity dictates, or may never need to be done at all. In the presence of an inoperable tumor and more especially in the presence of a recurrence, irradiation is often helpful.

Two complications, acute obstruction and perforation, may require prompt operation and may so obscure the diagnosis as to make it clear only when exploration has been carried out. Partial intestinal obstruction represents the major problem to be solved before the patient is fit for the removal of his growth. The authors believe that in the majority of cases the bowel can be safely and satisfactorily decompressed and cleansed without recourse to any sort of enterostomy. Should it appear after a reasonable interval that these measures have been ineffective and that the patient continues to exhibit signs of partial obstruction, surgical drainage of a proximal segment should be carried out. Preliminary drainage of the bowel may also be called for with patients who are poor risks by reason of age or of associated diseases.

In selecting the type of procedure for lesions in the colon, the principle generally adhered to in this series of cases has been aseptic end to end anastomosis following an adequate resection of the growth and its adjacent mesentery. Seventy-one cases of aseptic anastomosis of the Parker-Kerr or clamp type yielded a mortality of 11.2 per cent, while 19 cases of open anastomosis yielded a mortality of 26.3 per cent. Concomitant decompression in the absence of preliminary drainage should be used more frequently. In the management of the solitary, sessile polyp of the rectum having malignant characteristics with no gross or microscopic invasion of the muscularis mucosae, early local excision is performed. The patient is then carefully observed and, if there is evidence of recurrence of the polyp, excision is again performed. In attacking rectal cancer, radical removal of lymphatic structures must not be compromised.

The preference throughout this series has been for one stage abdominoperineal resection. Either during or immediately following a resection of the large bowel, the patient should receive as a routine procedure a transfusion of blood. Other intravenous fluids should be given in large enough amounts to insure an adequate urinary output.

Among 166 resections there were 23 deaths, or a mortality rate of 13.8 per cent. While only 56 per cent of the deaths are directly attributable to the operative procedure, the incidence of peritonitis is high enough to stress the importance of an aseptic type of anastomosis and the desirability for more frequent employment of concomitant bowel drainage.—S. G. Henderson.

Swinton, N. W., and Warren, Shields. Polyps of the colon and rectum and their relation to malignancy. J. Am. M. Ass., Nov. 25, 1939, 113, 1927–1933.

During the past ten years the treatment of carcinoma of the colon and rectum has been vastly improved. However, in reviewing a series of 300 patients with carcinoma of the colon and rectum, it was discouraging to find that the average duration of symptoms at the time of resection was nine months. This was the same duration that was revealed by a similar study five years previously.

In this paper the authors review a series of 156 patients with benign and malignant polyps of the colon and rectum who have been operated on at the Lahey Clinic during the past eight years. In this study the term polyp will include not only those pedunculated tumors arising from the wall of the large bowel but also those sessile tumors arising from mucous membrane which have no demonstrable pedicle. Clinically, mucosal polyps are classified as benign or malignant, single or multiple, and cases of multiple polyps are referred to as multiple polyposis. Histologically, the structure of polyps varies markedly. The covering epithelium ranges from the normal mucosa of the large intestine to irregular glands, variable in size and shape and lined with tall columnar epithelium with large, vesicular nuclei and prominent nucleoli frequently containing mitotic figures. The mucosa of the polyp always merges smoothly with that of the adjacent normal intestinal wall. The authors have found it possible to demonstrate histologically all stages in the sequence of change from normal colonic mucosa to actual adenocarcinoma.

The etiology of polyps of the colon and rectum has not been accurately established. Mc-Kenny obtained convincing evidence of the congenital nature of the cases of multiple polyposis of the entire colon. In the multiple poly-. poid-like structures which may develop in cases of ulcerative colitis the mucosa is never normal, nor is there the usual hyperplastic change seen in polyps. Following healing of the acute ulcerative process these pseudopolypoid tumors have been known to regress and disappear. The differentiation between ulcerative colitis in which polypoid changes have taken place in the mucous membrane and multiple polyposis associated with blood and increased amounts of mucus in the stool must be recognized. The majority of polyps of the large bowel are believed to be true tumors.

The location of the polyps found in this series is identical with the generally recognized distribution of carcinoma in the colon and rectum. Seventy per cent of the polyps were visualized through the 10 inch sigmoidoscope. The high incidence of multiple polypoid lesions, both benign and malignant, must be recognized and emphasized. In this series of 156 patients the polypoid lesions were multiple in 35 per cent, and in 121 cases malignant polyps were found. Polypoid disease may be found at any age and evenly distributed among males and females.

Polyps do not give rise to symptoms early in their development. As polyps become larger, the incidence of bleeding, mucus and rarely obstructive symptoms will be more frequent. Likewise the more extensive the involvement of the colon and rectum with polypoid disease, the greater the glandular development and the higher the incidence of bleeding and mucous discharges. In malignant polyps the symptomatology does not differ from that of the other types of malignant disease found in the large bowel. The importance of rectal bleeding, altered bowel function and the presence of unexplained abdominal pain in the early diagnosis of malignant disease is emphasized.

All patients with rectal and colon disorders should be examined by sigmoidoscope and by barium enema. The patient should be prepared for roentgen study by the use of castor oil and a cleansing enema. The use of the contrast air enema is helpful in localizing small organic lesions in the colon.

Microscopically, it is relatively difficult to determine the presence or absence of malignant change in intestinal polyps. Definite lymphatic or intravascular invasion nearly always means a clinical malignant condition. Different portions of the polyp may present entirely different histologic pictures. The entire polyp together with its base must be examined microscopically for an accurate diagnosis of malignancy. The visualization and palpation of polypoid structures are of the utmost importance in establishing their benign or malignant nature. Fourteen per cent of the malignant tumors of the colon and rectum can histologically be demonstrated to have arisen in benign mucosal polyps. All polyps of the colon and rectum should be regarded as pre-malignant lesions.

Removal or destruction by fulguration of all polypoid structures in the colon and rectum is necessary if one is to detect early malignant change and prevent subsequent development of carcinoma in this region.—S. G. Henderson.

### GENITOURINARY SYSTEM

ALBRIGHT, FULLER, SULKOWITCH, HIRSH W., and CHUTE, RICHARD. Nonsurgical aspects of the kidney stone problem. J. Am. M. Ass., Dec. 2, 1939, 113, 2049–2053.

The approach to this entire subject is based on the following major premise and its corollary:

Premise: A patient with urine of such composition that some crystalloid precipitates out of it is predisposed to the formation of a stone composed largely of the precipitated crystalloid (compare cystine stone in cystinuria, uric acid stone in gout and calcium phosphate or calcium oxalate stone in hyperparathyroidism).

Corollary: In a case in which there is a tendency for stones composed predominantly of a certain crystalloid to form, treatment should be directed to altering the composition of the urine in such a way that solution of the crystalloid is favored.

In addition to the foregoing propositions, stasis undoubtedly is a factor, while infection, although also a factor, probably plays its chief rôle by changing the composition of the urine.

There are four common types of kidney stones—calcium phosphate, calcium oxalate, uric acid and cystine. The urine should be made acid for calcium phosphate stones and alkaline for uric acid and cystine stones. With oxalate stones the pH of the urine is unimportant. Staghorn stones are nearly always composed of calcium phosphate or cystine. Very suggestive of cystine stones is the coalescence of several small stones

to form a large one. The lamellar structure of phosphate stones is often discernible in the roentgenogram. Hyperparathyroidism usually causes calcium phosphate stones but occasionally calcium oxalate ones. A structure suggestive of a snowflake with spicules radiating from a central focus is pathognomonic of calcium oxalate. Failure of the stone to show in the roentgenogram is strong evidence in favor of a uric acid stone.

The dissolution of stones is not an impossibility. By keeping the urine alkaline, a cystine stone in the kidney pelvis may be caused to disappear. Attempts to dissolve calcium phosphate stones by keeping the urine acid have usually been largely unsuccessful. The stones may not become larger, but seldom get smaller. The reason for the poor results is that acid regimens increase the amounts of phosphate and calcium in the urine and thus tend to make it saturated. Attempts have been made to inject some "dissolving" substance by the retrograde method. In one case in which there were multiple stones (believed to be calcium phosphate) in the urinary bladder, dissolution of the stones was brought about by injecting a solution of sodium citrate—citric acid at a pH of 4.0. This solution combines the effect of acids in dissolving phosphates with a specific effect of citrate in dissolving calcium salts by decreasing the calcium ion concentration. It is possible that results may be obtainable in dissolving this type of stone even in the kidney pelvis. Recent incomplete studies suggest that sodium hexametaphosphate solutions may be even more effective than citrate solutions. This substance will actually dissolve calcium oxalate in a test tube. - S. G. Henderson.

### SKELETAL SYSTEM

Spurling, R. Glen, and Bradford, F. Keith. Neurologic aspects of herniated nucleus pulposus at fourth and fifth lumbar interspaces. J. Am. M. Ass., Dec 2, 1939, 113, 2019–2022.

On the basis of the authors' experience with a series of 85 low intraspinal lesions treated surgically, they present what they have found to be the characteristic clinical picture of herniated nucleus pulposus at the fourth and fifth lumbar interspaces. Neoplasm along the course of the sciatic nerve, rectal or pelvic disease and disease of the osseous structures must be ruled out by regional and roentgenologic examinations.

The relations between the fifth lumbar nerve and the disc between the fourth and fifth lumbar vertebrae and between the first sacral nerve and the lumbosacral disc are especially important. The nerve roots forming the cauda equina are freely movable in the large lumbar canal except as they approach their exits, where they are fixed. Therefore displacement of the roots is possible, except near the port of exit, without neurologic deficit. The dural sleeve of the first sacral nerve separates from the thecal sac above the lumbosacral disc and can thus be compressed without deforming the sac. Recent studies indicate that there is a profuse supply of sensory nerve endings from the recurrent branches of the lumbar nerves in the annulus fibrosus and the posterior longitudinal ligament.

Symptoms. The occurrence of severe, persistent sciatic pain is of greatest importance diagnostically, especially if it is exaggerated by coughing, sneezing or straining. Points of greatest intensity are likely to be in the gluteal region, the posterior aspect of the thigh, the back of the knee or the lateral aspect of the leg or ankle. In almost every case incapacitating pain low in the back precedes the sciatic pain by weeks, months or years. The pain low in the back is variable or intermittent and is usually intensified by bending or lifting. Tingling, prickling, cold or numb sensations occurring below the knee in the lateral aspect of the leg or in the foot are characteristic of herniated nucleus pulposus at the fourth or fifth lumbar interspace.

Important clinical findings are a stiff lumbar spine, severe sciatic pain with a positive Lasègue sign, hypesthesia of the foot and lateral aspect of the leg and diminution or absence of the ankle jerk. Listing to one side is common. Limitation of flexion of the lumbar spine may be marked. Tests of the motor power are usually not of much aid because patients confuse pain on using the affected part with weakness. More important is diminution or absence of the ankle jerk, which usually occurs with herniation at the lumbosacral disc. The sensory changes are most important in making the diagnosis. Herniation at the fourth lumbar disc (involvement of the fifth lumbar and first sacral nerves) usually results in hypesthesia of the anterolateral aspect of the leg with inclusion of the great toe, while herniation at the lumbosacral disc (involvement of the first and second sacral nerves) gives hypesthesia of the posterolateral aspect of the leg with inclusion of the lateral aspect of the foot. Patients with herniation of the nucleus pulposus at the fourth lumbar and the lumbosacral disc have in common pain low in the back, severe sciatic pain, and hypesthesia or anesthesia below the knee. True sciatic pain is not caused by involvement of the ligamentous structures alone. If the nucleus pulposus extrudes through the annulus fibrosus without causing nerve compression the lesion remains in the category of purely ligamentous injury. The reliability of these neurologic symptoms and signs is attested by the fact that g consecutive herniations of the nucleus pulposus have been removed without confirmation with iodized oil or other contrast media.—S. G. Henderson.

Chamberlain, W. Edward, and Young, Barton R. The diagnosis of intervertebral disk protrusion by intraspinal injection of air; air myelography. J. Am. M. Ass., Dec. 2, 1939, 113, 2022–2024.

Gaseous contrast media have been used as a routine for the past three and one-half years with all patients who have had sufficient symptoms and neurologic evidence to cause suspicion of an intraspinal lesion. Oxygen is now used because it is absorbed faster than air and produces less discomfort. In an experience based on more than 300 spinograms, in each case in which operation was performed the exact level of the lesion determined by myelographic examination was verified by laminectomy.

The technique of injection varies somewhat, depending on the level of the lesion. The technique of and indications for injection at different levels are described. If a lesion is suspected below the third lumbar vertebra, with the head of the table lowered to an angle of from 20 to 25 degrees using an 18 or 20 gauge spinal needle inserted into the subarachnoid space at the second lumbar interspace, spinal fluid and air are exchanged in 5 cc. quantities until air escapes through the needle. In case the lesion is believed to be above the third lumbar vertebra, the spinal needle is inserted in the third lumbar interspace with the patient in a horizontal position and a Queckenstedt test is done. If this test shows a partial or complete block, from 3 to 6 cc. of spinal fluid is carefully replaced by an equal amount of air and the patient is examined in the sitting posture. If the Queckenstedt test is negative, the dorsal sac can be visualized by replacement of spinal fluid with air by either lumbar or cisternal puncture.

Visualization of air in the spinal canal depends on roentgenograms of good contrast and detail. "Overexposed" films give more information, so the kilovoltage is raised from 8 to 10 above that necessary for spinal detail. The minimal film requirements in the lumbar region are stereoscopic lateral and anteroposterior projections. In the upper dorsal or cervical region, it is advisable to take stereoscopic oblique projections as well as the lateral ones.

The diagnosis of a herniated disk depends in most cases on the indentation or encroachment of the limiting membrane of the subarachnoid space. The one exception to this is when the disk has produced a complete block of the canal. Here the inferior margin of the disk is easily demarcated by the air bubble trapped under it. The indentation of the air column due to a herniated disk is not always seen on the lateral projections. In a number of cases the defect was visualized only on the anteroposterior projections as a bilateral waist-like constriction or a unilateral marginal indentation. A major advantage of air and oxygen as contrast media for myelographic examination is the fact that their use does not entail leaving unabsorbable and possibly irritating substances in the spinal canal.—S. G. Henderson.

CAMP, JOHN D. The roentgenologic diagnosis of intraspinal protrusion of intervertebral disks by means of radiopaque oil. J. Am. M. Ass., Dec. 2, 1939, 113, 2024–2029.

Pathologic studies of protruded intervertebral disks indicate that the protruded fragments are composed of fibrocartilage, portions of the nucleus pulposus and occasionally remnants of the notochord. These structures are not ordinarily opaque to roentgen rays and for this reason the roentgenologist is dependent on the use of some contrast agent for the indirect visualization of the protrusion. Iodized oil, when employed under proper circumstances, has resulted in an accuracy of diagnosis that is shared by few other roentgenologic procedures. The chief objection to the use of iodized oil is that it is more or less of an irritant to the meninges and is contraindicated in the presence of inflammatory disease. The use of air or oxygen has much in its favor but there are certain decided disadvantages. Because of the difficulty in controlling the position and distribution of the air (or oxygen) its use with any satisfaction is restricted to the lumbar canal. The accuracy of

the diagnosis with air is not equal to that attained with iodized oil.

No contrast agent should be used unless the clinical and neurologic examination indicates the possible presence of an intraspinal lesion that cannot be localized by ordinary clinical procedures. Because air or oxygen is very difficult to hold in position in the thoracic or cervical portion of the spinal canal, and because the superimposition of the shadow of air in the trachea, larynx and pharynx renders the interpretation of resulting shadows exceedingly difficult or impossible, iodized oil is the medium of choice for the demonstration of lesions at or above the conus. The great majority of protruded intervertebral disks occur in the lumbar and lumbosacral regions where they are accessible to examination by either air or iodized oil. If air studies are negative, inconclusive or unsatisfactory, and the history and neurologic examination are suggestive of the presence of a protruded disk, iodized oil should be used to check the spinogram. In the interest of early diagnosis and for the localization of lesions before obstruction has occurred, it is necessary to use a quantity of iodized oil sufficient to fill the subarachnoid space completely at any desired level. Five cubic centimeters of iodized oil is the optimal volume for accurate and consistent localization of non-obstructing lesions.

The lumbar injection of iodized oil is preferred because it is easier and safer to carry out than cisternal puncture and will facilitate the keeping of the oil together as one mass in the lower part of the spinal column. The iodized oil used should be clear, transparent and only faintly yellow. Prior to injection the ampule is warmed to a temperature of 105° F.

It is desirable that the roentgenologic study be carried out as soon after the injection as possible. Some method of quickly recording the fluoroscopic image on films is highly desirable. If the result of the examination of the lumbar spinal subarachnoid space is negative, it is important to examine the subarachnoid space higher up. Fifty per cent of patients with tumors of the spinal cord located in the thoracic region and 30 per cent of patients with such tumors located in the cervical region have low back or sciatic pain or both as an associated or coincident symptom.

Usually the protruded fragment is situated in the anterior portion of the spinal canal and will produce its maximal effect on the column of iodized oil when the patient is lying in a prone or prone-oblique position. The classic defect is a sharply defined unilateral rounded indentation of the iodized oil shadow opposite an intervertebral disk. Midline protrusions when of moderate size may produce only a central defect. Except as the iodized oil deformity may be influenced by the presence of associated hypertrophy of the ligamentum flavum, the larger the protrusion the greater the obstruction of the subarachnoid space will be, and the greater the tendency to produce a bilateral deformity. Localized hypertrophy of the ligamentum flavum without coincident protrusion of a disk may imitate all the clinical phenomena of a protruded intervertebral disk and is characterized in the lateral view by a broad or rounded indentation on the posterior aspect of the column of iodized oil between contiguous laminae. In the prone or supine position the hypertrophy may be portrayed by broad indentation of the column of iodized oil, generally bilateral. When considerable hypertrophy of the ligamentum flavum accompanies a large protruded disk, the mass of iodized oil is compressed between the protruded disk anteriorly and the hypertrophied ligamentum flavum posteriorly and laterally. In about one-third of the cases of protruded intervertebral disk, lateral or posterior displacement of the nerve root shadows of the cauda equina or both will be visible at the site of the protrusion.

The significant symptoms of a protruded disk are the result of pressure exerted on the nerve roots by the protruded fragments. Edema of an affected nerve root may result in three ways: (1) by irritation of the root as it passes over the protruded disk, (2) by compression of the root between a protruded disk and the contiguous pedicle of the vertebra or (3) by compression of the root between a protruded disk and a hypertrophied ligamentum flavum. In the presence of an anomaly in which the cul-de-sac terminates higher than usual, it may be impossible to prove or disprove the presence of a protruded lumbosacral intervertebral disk by roentgenologic methods. It is interesting that all errors of interpretation occurred at the lumbosacral junction, where the spinal canal is relatively large and the diameter of the caudal sac may be small because of its fusiform termination. Under such circumstances even a large protruded disk may exist without indenting the sac.-S. G. Henderson.

Love, J. Grafton. Protruded intervertebral

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Analysis of more than 300 proved operative cases justifies the statement that laminectomy accompanied by removal of the protruded portion of an intervertebral disk is possibly the least radical of any known curative treatment for such a disabling condition. The characteristic symptom complex for protruded lumbar intervertebral disks is as follows: Complaint of intractable low back and sciatic pain. On examination, spasm of the lumbar muscles, loss of the normal lumbar lordosis, positive Lasègue's and Kernig's signs, sciatic tenderness and diminution or absence of the homolateral Achilles' tendon reflex. A moderate elevation of the total protein content of the cerebrospinal fluid. Narrowing of the fourth or fifth lumbar intervertebral space.

In spite of one's ability to diagnose the lesion accurately without the use of a contrast medium, in some cases routine employment of a contrast medium acts as a safeguard against overlooking multiple lesions, and enables the surgeon to perform as short a laminectomy as possible. However, direct exploration for protruded disk on the basis of a clinical diagnosis may be advisable even in the absence of positive roentgenologic findings.

Before undertaking such an operation, it is essential to know what disks are most likely to be involved and it is well to bear in mind that 10 per cent of all lesions were multiple in the series in which operation was performed. Ninetysix per cent of all protrusions in the aforementioned 300 cases occurred at the third, fourth or fifth lumbar vertebral interspace. In 84 per cent of the 300 cases the protrusions occurred at the fourth or fifth lumbar interspace. A removal of the laminae of the fifth lumbar vertebra and a resection of the fourth and fifth lumbar ligamenta flava will result in adequate exposure. If there is a protruded disk, its presence usually will be signalized by a marked thickening of the ligamentum flavum at that particular interspace. The important point to remember about the ligamentum flavum is that although it may be of sufficient size to compress the nerve roots, causing intractable pain, this phenomenon without an associated protrusion of the disk is rare. In 300 patients who had proved protruded disk, there were encountered only 12 cases of hypertrophy of the ligamentum flavum without an associated disk protrusion.

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LOVE, I. GRAFTON. Protruded intervertebral

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Before undertaking such an operation, it is essential to know what disks are most likely to be involved and it is well to bear in mind that 10 per cent of all lesions were multiple in the series in which operation was performed. Ninetysix per cent of all protrusions in the aforementioned 300 cases occurred at the third, fourth or fifth lumbar vertebral interspace. In 84 per cent of the 300 cases the protrusions occurred at the fourth or fifth lumbar interspace. A removal of the laminae of the fifth lumbar vertebra and a resection of the fourth and fifth lumbar ligamenta flava will result in adequate exposure. If there is a protruded disk, its presence usually will be signalized by a marked thickening of the ligamentum flavum at that particular interspace. The important point to remember about the ligamentum flavum is that although it may be of sufficient size to compress the nerve roots, causing intractable pain, this phenomenon without an associated protrusion of the disk is rare. In 300 patients who had proved protruded disk, there were encountered only 12 cases of hypertrophy of the ligamentum flavum without an associated disk protrusion.

If the patient's symptoms are mild and do not interfere to any great extent with his usual activities, some one of the more common therapeutic measures may be employed. If the patient is very uncomfortable or is experiencing enough trouble to warrant bed treatment for two weeks, surgical treatment of the lesion should be advised. If radiopaque oil is used to localize the lesion, it should be injected into the lumbar segment and the roentgen examination should be carried out on the day of operation.

Recently the author has employed air in the subarachnoid space as an aid to roentgenologic localization of protruded discs, but the accuracy achieved by this method in his hands has not approached that resulting from the use of radiopaque oil.—S. G. Henderson.

Freiberg, Joseph A. Low back pain. J. Am. M. Ass., Dec. 16, 1939, 113, 2195-2198.

For years many orthopedic surgeons believed that the problem of low back pain was simple and that it was merely a question of differentiation between lesions in the lumbosacral area versus sacroiliac joints. However, there was actually a third lesion, the herniated or protruded intervertebral disc, previously unrecognized in its frequent rôle as a cause of low back pain and sciatica. At the same time that the herniated disc syndrome has become better known, so also have the intricate and less obvious muscular and fascial lesions about the lower part of the back, pelvis and thigh yielded to clinical and scientific study. In many cases early surgical treatment is to the great advantage of the patient, but in other series careful study of the individual patient will show that ionsurgical therapy alone is indicated in from lo to 90 per cent of the cases. An active infecious lesion should be treated conservatively and painful or unstable joint due to a pre-existing nfectious process must be immobilized either y muscular or mechanical support or by operaive fixation.

The real diagnostic problem in low back pain, with or without sciatica, is to differentiate between the primary and secondary causes for the ain and to evaluate their relative significance with regard to therapy. Dissimilar lesions may e and are associated with similar types of muses spasm responses. Likewise, as the muscle pasm, per se, may be painful or may cause secondary painful areas, it is frequently difficult to fferentiate between the primary lesion causes the muscle spasm and the secondary lesion,

which is sometimes the true cause of the pain. The primary lesion associated with low back pain may be a true joint lesion, synovitis, a ligamentous trauma, periostitis at the site of muscle origin or insertion, myositis, fasciitis or a lesion of the intervertebral disc.

Before an attempt is made to treat a syndrome involving low back pain the lesion must be identified. The history of the mode of onset is especially important. In many cases the history will clearly bring out the fact that there was a single site of pain and tenderness, subsequently masked by the gradual development of secondary symptoms. The story of something slipping or snapping usually indicates a ligamentous or periosteal tear which may well be the lesion to be treated.

In the presence of acute low back pain with or without sciatic pain an extensive physical examination accompanied by forceful testing of the range of mobility of the various joints is definitely contraindicated. Observation and palpation will elicit the location of the areas of tenderness and injury. The more severe low back injuries may be accompanied by lesser fractures involving articular processes, laminae or pedicles. Lesions such as ruptures of the annulus fibrosus and consequent posterior protrusions of the intervertebral discs and the less frequent lesions of the ligamentum flavum followed by hypertrophy or cicatricial thickening of the ligament may occur and may be associated independently with constant or recurring attacks of low back pain. It may be assumed that many conditions about the lower part of the back are capable of causing painful manifestations and that because of the intricate mechanism of this region no one type of lesion can be accepted as the chief etiologic factor.

Acute aggravation of pain in the lower part of the back, buttock or sciatic nerve area accompanying sneezing or coughing may be due to a protruded disc or other mechanical pressure on the nerve root, or to spasmodic contracture of the abdominal and back muscles where there are lesions of the fasciae, muscles or joints. Relief from pain and disappearance of muscle spasm on lying down generally imply that a postural or abnormal mechanical strain has been removed from a lumbosacral or sacroiliac joint. The significance of the straight legraising or Lasègue test is discussed. The Ober test for contractured thigh fascia may be positive as the result of muscle spasm involving the tensor fasciae femoris and gluteal muscles. The

Ely, or prone knee flexion, test is one of the most valuable maneuvers to demonstrate the existence of thigh fascial contractures but not of a lumbosacral lesion, as originally described. Probably the most valuable of all the tests in determining the exact site of periosteal, ligamentous or joint lesions is the localization of one or more areas of definite tenderness on palpation when the patient is lying comfortably on a firm table. Relief of pain on injection of procaine hydrochloride usually demonstrates the fact that the lesion involves periosteal or ligamentous tissues previously the seat of a trauma or inflammatory process. In both neurologic and roentgenologic studies the spinal studies must be correlated with the other clinical data. -S. G. Henderson.

Engel, D. Dysostosis multiplex: Pfaundler-Hurler syndrome. *Arch. Dis. Childhood*, Sept., 1939, 14, 217–230.

In 1919 Hurler described in detail 2 cases of dysostosis multiplex which had originally been reported by Pfaundler. They displayed the following unusual combinations of congenital anomalies: clouding of the corneas, a deformity of the skull (oxycephaly), a disproportionate dwarfism strongly resembling that of hypothyroidism (with some of the usual signs of that condition such as saddle nose, mental defect, dry skin, inguinal and umbilical herniae, crura valga and pedis valga), contraction of the fingers, limitation of movement in other joints and defective hearing. Pfaundler suspected he was dealing with a new syndrome and since then twenty other cases have been reported, showing the same combination of anomalies.

Engel's patients were two brothers, native Chinese, and he believes them to be the first cases of this condition observed in China. In addition to the other anomalies described in the literature, the brothers had bilateral congenital elevation of the scapulae, Sprengel's deformity. He considers the name of dysostosis multiplex to be more suitable than the previously proposed term, gargoylism.—R. S. Bromer.

TRAUB, ERICH. Epiphyseal necrosis in pituitary gigantism. Arch. Dis. Childhood, Sept., 1939, 14, 203-216.

Traub reports a case of pituitary gigantism. The patient's roentgenograms showed multiple epiphyseal necroses. The changes noted were a typical osteochondritis deformans of the right hip joint, Köhler's disease of both tarsal scaph-

oids, changes in the bodies of the vertebrae and epiphyseal necrosis in the heads of the first metatarsals. Traub thinks that these abnormalities were caused by endocrine dysfunction. Osseous involvement resembling Perthes' disease has been described in the literature in cases of adiposogenital dystrophy, in hyperthryoidism, in cretinism, in pituitary dwarfism and in gigantism.—R. S. Bromer.

Knutsson, Folke. Die röntgenologische Frühdiagnose der Rachitis. (The early roentgen diagnosis of rickets.) *Acta paediat.*, 1939, 24, 403–421.

Knutsson examined roentgenologically the hands and feet and the anterior borders of the ribs of premature infants during their first year of life. In 36 cases he found rachitic changes. In 10 of these cases the rachitic changes were confined to the ribs only, the other metaphyses being normal. In 18 cases the rib ends were affected earlier than the other metaphyses and in 17 cases the ribs ends showed changes simultaneously with the distal ends of the diaphyses of the ulnas.

He believes that in many instances the rachitic process is fully manifest in the rib ends when the distal ends of the ulnas show only early or slight changes. Again changes may be present in the ribs and the skeleton elsewhere will show no roentgen evidence of the disease. The ends of the ribs become deformed very early, the most pronounced change being cupping or assumption of a beaker shape. In the ulna and fibula, the earliest change consists of a beginning bowl-shaped deepening of the metaphyseal border with a blurring of its contour. In the tibial metaphysis, the first sign is a tendency to spur formation of the metaphyseal border and the beaker shape or cupping is a later development.

Knutsson employs an oblique projection of the central ray for demonstration of the anterior ends of the ribs and thus prevents the overlapping of the shadows of the ends of both the right and left ribs which is found in straight lateral views.—R. S. Bromer.

### ROENTGEN AND RADIUM THERAPY

Proske, Eva. Untersuchungen über Ösophagusmetastasen. (Studies on metastases into the esophagus.) *Strahlentherapie*, 1939, 64, 227–248.

In the material of the Roentgen Institute of the University of Zurich the author observed in tumors of the pharynx in which the primary tumor could be made to disappear chiefly by the use of the protracted fractional irradiation, the frequent development of secondary esophageal tumors.

The secondary esophageal tumors were observed chiefly in deeply situated mesopharynx tumors as well as in tumors of the posterior wall of the hypopharynx.

Secondary esophageal tumors were never observed when the primary malignant tumor was situated in the larynx and in the epipharynx. Secondary esophageal tumors are rare also in primary carcinoma of the mouth cavity.

Twenty-one cases of secondary esophageal tumors were found in 382 cases of meso- and hypopharynx tumors; one of these tumors was found before the discovery of a hidden mesopharynx tumor, 3 were found at the beginning of treatment of the pharyngeal tumor and the remainder only after the completion of the treatment of the primary tumor. The statistics presented above, however, give an erroneous picture since many patients died before the esophageal metastasis came to manifestation. A more reliable picture is obtained when the frequency is computed on the basis of patients rendered free of symptoms who are still alive or who have died as a result of distant metastases. Using this as a value a frequency of 16 per 141 patients during a period of observation of two years is obtained. This represents a frequency of about 11 per cent. It appears even more plausible to assume that every sixth to seventh patient who has been treated or cured of a meso- or sypopharynx tumor develops or dies from a secondary esophageal tumor.

The secondary esophageal tumor is always observed in carcinoma and never in sarcoma.

In 9 cases the histologic structure was identical with that of the primary tumor and in I case it was different.

No relationship exists between the size of the primary tumor and the appearance of the secondary esophageal tumor.

No relationship exists between the appearance of the tumor in the esophagus and regional netastasis of the pharynx tumor and the beginning of treatment.

The most frequent seat of the metastasis into the esophagus is the middle and lower third of the esophagus.

No relationship exists between the appearance of distant metastases outside of the sophagus and the secondary esophageal tumor.

In a predominant number of cases the secondary esophageal tumors appear as inoculation metastases in the esophagus. The lymphogenous mechanism of origin is rare.

The prognosis is hopeless.

The treatment is palliative and best results are obtained from roentgen therapy followed by radium.

The fact that esophageal metastases in the author's material were found even more frequently in association with a small primary tumor than with a large one suggests the possibility that the exploratory excision of part of the tumor favors the inoculation and may actually be responsible for it. In consideration of the above it would be very advisable to carry out the exploratory excision, if possible at all, by means of the electrosurgical loop.—A. S. Schwartzman.

Mallet, Lucien. Über die Teleröntgentherapie von Krebsmetastasen. (Teleroentgen therapy of carcinoma metastases.) *Strahlentherapie*, 1939, 64, 201–218.

An attempt was made by this author to utilize teleroentgen therapy for the treatment of distant metastases, especially of bone metastases. This task, which seemed impossible of solution a few years ago, could again be considered with the recognition of the fact that the organism can tolerate whole radiations or half radiations when only slight individual doses are chosen and when the treatment is extended over a long period of time.

This newly recognized fact was utilized at first in the treatment of blood diseases, especially of lymphatic and myeloid leukemia, erythremia and especially of lymphogranulomatosis. Especially in the last mentioned disease it was found that after relatively very small doses distributed over the entire body the glandular enlargements disappeared.

It appeared conceivable also that some epithelial tumors could be successfully attacked by this method. Daily small doses given over a long period of time and distributed over the entire body were hitherto considered unsuitable because most radiologists were of the opinion that only the so-called cancericidal dose alone was effective.

Since the metastasis and generalization represent characteristic properties of carcinoma, an attempt must be made to adjust the radiation technique to this fact. Hitherto only local radiations were carried out. Clinical experience

has taught, however, that carcinoma is not a local disease and that even small originally operable and movable tumors metastasize relatively early. As mentioned previously, however, no attempt was made for a long time to treat the entire body because of the idea of cancericidal dose.

In 1932, however, Mallet determined clinically and experimentally that daily irradiation of a large region of the body with small doses are well tolerated by the individual. He further found that certain generalized carcinomas such as seminoma and myeloma can be destroyed by roentgen doses which were considered hitherto absolutely insufficient for the destruction of a tumor. The basis of teleroentgen therapy is as follows: The treatment of the primary tumor and of all its metastases is carried out by irradiation of large body regions, including the bony system, glandular tissues and viscera. An attempt is made in this form of therapy to obtain a cure of the carcinoma by means of a minimal dose of roentgen rays and an attempt is made to prevent, if possible, any injury to the hemopoietic system. Care is exercised also not to injure the skin and connective tissue in that daily only very small partial doses are used. Experience has shown that even minute doses have a definite detrimental effect on carcinoma. The effect of teleroentgen therapy is based on three physical conditions: The great distance, the large radiation field and the strong depth effect. An extensive region of the body is more or less uniformly permeated by roentgen rays. All body regions in which carcinoma metastasis is suspected are irradiated with the same amount of rays. The distance of the source of the roentgen ray must be so large that the rays fall practically parallel. The skin focus distance must be at least I meter and in some cases it actually varies from I to 3 meters. The field size on the skin must be at least 40 × 40 cm. The above represents basically teleroentgen therapy. One of the prerequisites for satisfactory results of teleroentgen therapy is the distribution of small doses over a very long period of time. The author irradiates his patients mostly daily but at least four times a week if the general condition of the patient permits it. The treatment of the thorax requires, for instance, at least 30 to 40 individual irradiations; that is, a duration of treatment of about two months where the patient is given daily about 25 r. When the entire body has to be treated a duration of four to five months is necessary.

Since 1933 over 600 cases of carcinoma have been treated by Mallet by teleroentgen therapy; the carcinoma was represented by extensive glandular infiltrations in the axilla, in the infra- and supraclavicular and cervical regions, in the mediastinum and in the pelvis, as well as by multiple bony metastases including the spinal column, pelvic girdle and upper and lower extremities. Even though statistical data cannot be offered which would show in a clear cut manner that many of these patients have been cured, nevertheless it can be definitely shown that in most of the patients treated by this method life was prolonged and the symptoms were ameliorated.—A. S. Schwartzman.

Mardersteig, Klaus. Röntgenschädigung und Blutbild. (Roentgen injury and blood picture.) Strahlentherapie, 1939, 64, 311–317.

It has long been known that the hemopoietic organs are especially sensitive to roentgen rays. An individual is endangered even when exposed to the influence of very minute amounts of radiation in the course of a number of years; even under these conditions such minute injuries may lead to severe blood diseases such as aplastic anemia, myeloid and lymphatic leukemia. Even though the relationship between the radiation effect and anemia can no longer be doubted, the same does not hold true in regard to leukemia. Cases where roentgenologists have died from leukemia, of the myeloid or lymphatic type, are not as numerous as death due to anemia. Recent studies have contributed considerably to our knowledge of the white blood picture. Gansslen demonstrated regional differences in the normal white blood picture and has shown that the normal range of variation of the total leukocyte count as well as of the differential count is greater than hitherto stated even in textbooks. Gansslen carried out his studies on numerous patients as well as on a number of healthy individuals. From a study of 160 healthy maids he found that the white count under normal conditions varies not between 6,000 and 8,000 as hitherto stated, but between 3,500 and 9,000 and that the lymphocyte percentage varies not between 20 and 25 as hitherto assumed, but between 20 and 45. The lowest leukocyte count under normal conditions was found by him to be 2,700 and the highest lymphocyte count under normal conditions was found to be 50.5 per cent. In 40.6 per cent of these 160 healthy maids, a leukopenia was found. More or less similar results were ob-

surgical removal or at necropsy. In this series there were 65 cases of these two types of ulcerative colitis, a substantial group, representing 13 per cent of the entire series. It is our feeling that the type of ulcerative colitis represented by these 65 cases has largely led to much of the confusion of the real nature of ulcerative colitis in which the precise etiologic factor has been doubtful or in dispute. In 1930, we reported a small group of cases of · chronic ulcerative colitis in which the distribution of the ulcerative process in the intestine was atypical. For these we used the designation "regional migratory ulcerative colitis." Some of these would now be classified as type 2 ulcerative colitis, and certain cases of "regional entero-colitis" would also be included in this group at the present time.

Type 4. This group includes those cases of ulcerative colitis in which the disease was considered to be due to infection of the intestine with Mycobacterium tuberculosis. Table IV shows the extent and distribution of the pathologic intestinal changes as revealed by roentgenologic examination.

Type 5. This group includes those cases in which the ulcerative colitis was considered to be due to infection with Endamoeba histolytica. It includes those cases in which actual organic changes were revealed in the intestine either at proctoscopic or roentgenologic examination, or both, as well as cases in which no such changes were demonstrated. The extent and distribution of the pathologic changes in the intestine as revealed by roentgenologic examination are shown in Table IV.

Type 6. This group includes those cases of atypical ulcerative colitis in which the pathologic and clinical manifestations differ from those of other types. In these cases the disease is considered to be part of the syndrome of one of several forms of dietary insufficiency.

Type 7. This group includes those cases of ulcerative colitis in which the involvement is practically always limited to the rectum and lower part of the sigmoid

colon. The etiologic background is considered to be the same as that in cases of ~ lymphogranuloma venereum.

Combined types. In but 7 cases in this series were two etiologic factors considered to be operating simultaneously to produce a mixed type of chronic intestinal infection. In 6 of the 7 cases Endamoeba histolytica was found to be present, in the stools, while the clinical and pathologic evidence pointed clearly to the coexistence of type I (thrombo-ulcerative) ulcerative colitis.

#### CLINICAL CONSIDERATION

The allocation of a given case of chronic ulcerative colitis into one of the types enumerated is usually done very readily, but sometimes it becomes a very difficult task. In general it may be said that the diagnosis is made by critical analysis of the history and the findings at physical examination and by correlating these with the objective evidence of intestinal disease as revealed by proctosigmoidoscopic and roentgenologic examination. Buie has contributed particularly vivid descriptions of the pathologic appearances of these ulcerative processes as the proctosigmoidoscope reveals them. He expressed the opinion that certain gross morphologic features are pathognomonic of certain etiologic types of ulcerative colitis. Intimate association with Buie and his colleagues in the Section on Proctology of the Mayo Clinic for many years permits us to confirm the validity of his opinion. The importance of the evidence yielded by expert use of the proctosigmoidoscope and by correct interpretation of the findings in the light of a large experience cannot be estimated too highly. The evidence of the competently performed and carefully interpreted roentgenologic examination ranks next in importance. In certain types of ulcerative colitis the roentgenologic manifestations are only somewhat less definitive than the proctosigmoidoscopic manifestations. Roentgenologic evidence assumes the primary position of importance when characteristic

tively normal segments between those seyerely diseased. No common bacteriologic orother etiologic agent has been determined for this form of ulcerative colitis.

. Type 3. In this group were placed those cases of chronic ulcerative colitis in which the lesion was similar in all pathologic respects to that described as type 2, except that those segments within reach of the proctosigmoidoscope were involved either alone or with segments of the colon above this level (Table IV).

The pathologic changes in the last two types of chronic ulcerative colitis present no clinical features by which they may be distinguished from each other consistently, and they are not to be distinguished from each other pathologically except by the distribution of the ulcerative process in the intestine. The division into two types was made chiefly for purposes of study. In ulcerative colitis type 3 a more complete and detailed pathologic picture is made available by the proctosigmoidoscope; in ulcerative colitis type 2, patho-

TABLE III

COMPARISON OF ROENTGENOLOGIC DIAGNOSIS AND ULTIMATE DIAGNOSIS IN 442 CASES IN WHICH ROENTGENOLOGIC EXAMINATION WAS MADE

Type as de- termined by roentgeno- logic exami- nation		Type—ultimate diagnosis									
	Total	I	2	3	4	5	6	7	Com- bined types		
I	261	243	4	8			_	2	4		
2-3	41	3	13	20	I	2		I	I		
4	IO				IO						
5	19	I		2	I	14			I		
6 7	I						Ι				
Negative	110	65		ΙΙ	I	32			I		
Total	442	312	17	4 I	13	48	I	3	7		

logic information is obtained less directly since it is deduced from roentgenologic data, although some detailed pathologic information has been obtained in those relatively few instances in which specimens were made available for study by

Table IV Extent of lesion as revealed by roentgenologic examination, in the various types

Extent of lesion	Туре											
	I		2		3		.4		5			
	Cases	Per cent										
Rectum—sigmoid	25	7.5										
Rectum—splenic flexure	26	7.8										
Rectum—hepatic flexure	28	8.4										
Rectum—cecum	169	51.0										
Cecum			` 4	23.5			3	21.4	6	7.7		
Cecum—ascending colon							4	28.6	4	5.1		
Cecum—hepatic flexure			I	5.9	4	8.3			,	3.1		
Cecum—splenic flexure			6	35.4	6	12.5	I	7.I	3	3.8		
Cecum—sigmoid			3	17.6						0		
Scattered distribution			3	17.6	6	12.5						
E- re colon					I 2	25.0	4	28.6	5	6.4		
Rectum—recto-sigmoid Rectum					7	14.6						
	(				6	12.5						
Negative No examination	65	19.6							34	43.7		
	19	5 · 7			7	14.6	2	14.3	26	$33 \cdot 3$		
Total	332	100	17	100	48	100	14	100	78	100		

TABLE I
DISTRIBUTION AS TO TYPE

Type	Number	Per cent		
I	332	66.4		
2	17	3·4 9.6		
3	48			
4	14	2.8		
5	78	15.6		
6	I	0.2		
7	3	0.6		
Combined	7	I . 4		
Total	500	100.0		

of this kind with this particular relationship in time to our entire series made it possible to take matters like these into consideration, because we have had the privilege of observing many of the patients on two or more occasions over a period of at least four years.

#### CLASSIFICATION

On the basis of bacteriologic and parasitologic, pathologic and clinical examinations, it was found that each of the cases of this series could be placed into one of seven types (Table 1) which have been designated as follows:

Type 1. Into this group were placed those cases in which the patients had the disease commonly known as "chronic ulcerative colitis," "colitis gravis," "idiopathic ulcerative colitis" and by various other names. Buie and Bargen have suggested the term "thrombo-ulcerative colitis" as a more suitable name for this type of chronic ulcerative colitis. We consider a characteristic streptococcus to be the primary inciting organism. In our experience, this is by far the most commonly encountered type of ulcerative colitis (Table 1). Of all the types of ulcerative colitis, it has the most consistent and most typical clinical, pathologic and hence, proctoscopic and roentgenologic manifestations (Tables II and III). The intestinal wall is diffusely involved. Earliest and severest manifestations appear in the rectum and lower segments of the colon. The disease tends to spread diffusely upward until the entire colon, even the lower part of the ileum, becomes involved (Table IV). Because of its relatively very high incidence, 66.4 per cent in this series, and because of the consistency with which its clinical, proctoscopic and roentgenologic manifestations conform to a certain pattern, we are inclined to use this type of ulcerative colitis as a norm and to describe other types chiefly by noting in what respects they differ from it.

Type 2. In this group were placed those cases of chronic ulcerative colitis in which the condition differed pathologically from that of type I (thrombo-ulcerative colitis) chiefly in that those segments within reach of the proctosigmoidoscope were not involved in the pathologic process. The existence and extent of the lesion was revealed at the roentgenologic examination (Table IV). The roentgenologic appearance of the diseased intestine may resemble that of any other form of ulcerative colitis very closely, or the diseased intestine may have a different, almost distinctive roentgenologic "look." Involvement may be diffusely spread over the entire colon, not including the rectum and sigmoid, or it may be irregularly distributed with rela-

TABLE II

COMPARISON OF DIAGNOSIS AS MADE BY PROCTOSCOPIC
EXAMINATION AND ULTIMATE DIAGNOSIS IN 464
CASES IN WHICH PROCTOSCOPIC EXAMINATION
WAS MADE

Type as determined by proctoscopic examination		Type—ultimate diagnosis								
	Total	I	2	3	4	5	6	7	Com- bined types	
I 2	323	309		- 6	I	2	I		4	
3	48	17		27		3			I	
4	I			I						
5	4 I	2		6	I	30			2	
7	3							3		
Negative	48	2	15	6	2	23				
Total	464	330	15	46	4	58	I	3	7	

## FORMS OF ULCERATIVE COLITIS

## CORRELATION OF CLINICAL AND ROENTGENOLOGIC DATA\*

By HARRY M. WEBER, M.D., Section on Roentgenology, and
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TT BECOMES more and more evident as experience accumulates and as diagnostic criteria become more precise that it is better to use the term "chronic ulcerative colitis" in a broad sense to denote a general clinicopathologic syndrome than to use it in a narrow sense to denote some one of the several specific disease entities in which this syndrome is developed. The term will be used in the broader sense in this paper. The syndrome of chronic ulcerative colitis may develop as a result of infection by one or more of several bacterial and animal parasites, or in association with certain dietary and constitutional deficiencies, or as a result of poisoning with certain chemicals. In medical practice it becomes necessary to distribute cases of chronic ulcerative colitis according to etiologic types, and the first and most fundamental clinical effort is directed at determining the specific etiologic factor responsible for the development of the syndrome, so that a more rational therapy may be instituted.

To determine the relative incidence of the various etiologic types of chronic ulcerative colitis which have come under our observation, and to test the validity of the diagnostic criteria by which we have been assigning our cases into these types, we have undertaken a statistical analysis of the case histories of 500 consecutive patients who came to the Mayo Clinic in the twenty-six months from February, 1933, to April, 1935, and whose clinical records had been entered in our statistical files under the designation of "ulcerative colitis." Bargen, Jackman and Kerr, in a paper entitled "Studies on the life histories of patients with chronic ulcerative

colitis," made an analysis of a large series of cases in which the disease was of streptococcic type. It was one of their aims to define the clinical pattern of this type of . chronic ulcerative colitis within sharper limits, thus to provide a more reliable guide for future classification of this and closely related intestinal diseases. They deliberately excluded from consideration all cases in which the disease was not clearly of this one type as determined by careful clinical, bacteriologic, proctoscopic and roentgenologic appraisal, as well as those cases in which the disease was proved to be of tuberculous or amebic origin. The group of cases we have selected for study differs from theirs chiefly in that it is a consecutive series and embraces all etiologic types of chronic ulcerative colitis coming to us in a relatively short, but we think a fairly representative, period of time. We chose a series of this kind for several reasons. In the first place, our experience with some of the more rarely encountered types of ulcerative colitis had accumulated sufficiently to enable us to formulate a somewhat more precise set of diagnostic criteria to be applied to them. Secondly, we had observed that the clinical and morphologic manifestations of even the more familiar types of ulcerative colitis varied, at times widely, with stage and virulence of the infectious process, with extent of intestinal involvement, and with presence or absence of complications. Thus, in some instances the manifestations were observed to become more typical at a later time; in others the ultimate diagnosis had to be made on the basis of the response to a more or less specific line of therapy. Our selection of a series of cases

<sup>\*</sup> Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19-22, 1939.

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### CLINICAL CONSIDERATION OF THE STOMACH\*

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CLINICAL consideration of the stomach is such a broad subject that it is obvious that I can only briefly discuss a few of its clinical aspects.

One condition which I feel merits much more consideration than it has received in the past is the symptom complex called pylorospasm. Pylorospasm might be defined as a spastic contraction of the thickened circular stomach muscle coat known as the pyloric sphincter, which at times produces various gastric disturbances.

Even though the definition seems fairly simple our knowledge of the causes of this condition is very limited. The reasons for this are more or less obvious. In the first place, the stomach of the intact human subject is quite inaccessible and studies under normal and abnormal conditions are chiefly by indirect methods. In general the methods of study are limited to: (1) the correlation of clinical symptoms with the pathological findings so well brought out in about 1830 by Cruveilhier; (2) by direct observation during surgical operations; (3) direct observation of the pylorus through gastrostomy openings such as done by Beaumont over one hundred years ago and recently by Carlson; (4) visualization of the stomach by means of the roentgen

ray, following various procedures such as the giving of certain foods and drugs and noting their effects; (5) gastroscopic examination.

Other reasons for our lack of knowledge of this subject are that the physiological control of the pylorus is very complex and its response to stimulation is dependent upon the state of the organ at the time it is stimulated. The results obtained experimentally depend upon such conditions as the strength and frequency of the stimulus and the level of the tone of muscle at the time. The sympathetic component of the vegetative nervous system is generally considered to be inhibitory to the pyloric sphincter and the vagus motor in its action, but an opposite effect may be obtained from either nerve, the tonus at the time appearing to be a determining factor.

Thus it is quite evident that this variability of response seems to be characteristic of gastric nerves and this in turn may help us better to understand the so-called paradoxical effects we get with certain drugs at times. Also, a better knowledge of the chemical as well as nervous control of physiological function and the manner in which it may be altered both physically and psychically may lead us far forward

<sup>\*</sup> Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

in the understanding of the variability of symptoms. This is certainly the rule in clinical medicine.

The etiologic factors in pylorospasm may be (a) intrinsic or (b) extrinsic.

- (a) Under the intrinsic causes the most common is a peptic ulcer of the stomach or duodenum.
  - (b) Under extrinsic causes we have:

Reflex factors due to organic lesions outside of the stomach, such as the presence of gallstones, which in themselves may be producing no localizing symptoms at times but only this so-called indigestion picture. It is often stated that gallstones may remain for a period of years in the gallbladder without producing any symptoms. If we will amplify this statement by adding the phrase "symptoms referable to gallbladder" we will then be much more accurate, because if a careful history is taken it well be found that often such patients have had attacks of so-called acid stomach or indigestion. Waiting for severe pains in these cases before removing the stones does not seem to be warranted. Pylorospasm may be produced by a slight change in position of the stones.

Appendicitis is another important cause of pylorospasm. Renal calculi, pyelitis, and diseases of the genitalia are others.

Reflex symptoms due to functional disturbances in other organs may occur as in the so-called irritable colon. Smith and his coworkers feel that the localized epigastric distress commonly associated with this irritability of the colon is gastric in origin and is brought about by reflex stimulation of the stomach.

Such findings agree with the observations of Carlson on animals that sufficient stimulation of all sensory visceral nerves may produce a contraction of the pylorus. Clinically, one wonders if these are not both local expressions of a constitutional defect, and that the particular organ or structure having the lowest threshold is the one which produces symptoms. Biliary dyskinesia may be another symptom complex explained in the same manner.

Under systemic causes of pylorospasm one can include:

- (1) Allergic states brought about by the ingestion of some of the more common offenders, as milk, eggs and shell fish, to which the particular individual is sensitive. The same findings as in bronchial asthma occur, namely, spasm of smooth muscle and edema of the mucous membrane.
- (2) Toxic states caused by the excessive use of tobacco.
- (3) Endocrine disturbances. Symptoms of dysfunction as manifested at the time of menstruation and the menopause are commonplace. The signs and symptoms associated with the neuromuscular imbalance in both hyperthyroid and hypothyroid states often are encountered.

Diseases of the central nervous system such as tabes dorsalis may be an occasional cause. Gastric crises examined roentgenologically during an attack may show nothing but a pylorospasm.

An organic lesion of the brain such as a tumor may be another productive agent.

Psychoneurosis as a cause of pyloropasm possibly occurs with much greater frequency than is at present suspected.

If the spasm is of short duration in any one of these conditions there may be no dilatation of the stomach, but if persistent and prolonged, a dilatation may occur due to the associated hyperperistalsis and hypersecretion.

It is obvious from the foregoing that, clinically viewed, our methods of study for the diagnosis of pylorospasm are limited to a very few procedures.

It can be seen, therefore, that there must be close cooperation between the clinician and the roentgenologist.

A careful history and its proper interpretation are of great importance because there may be nothing abnormal on physical examination even in the presence of either a functional or an organic disturbance of the gastrointestinal tract.

Further, one must have some understanding of the mode of production of the patient's subjective complaints and the way in which they may be modified by his environment.

There are facts brought out in the history which in some cases may be of great importance to the roentgenologist in his recognition of early pathology. In turn, the diagnosis of the clinician is verified or disproved. If organic changes are present the exact position of the pathological lesion is brought out, and if surgical measures are indicated they can be carried out at an early date, allowing a distinct advantage in prognosis. The clinician is also able to follow the results of his therapy by routine examination in selected cases.

Another condition which I desire to bring to your attention is the seasonal incidence of the symptomatology in peptic ulcer. Moynihan many years ago emphasized it and stressed the constitutional type of individual in which it occurred.

Einhorn also stressed it and brought out the fact that certain definite times of year seemed to be critical periods. Seventyseven per cent of his cases occurred in the spring and fall. If one will follow his own ulcer case histories he will find that in the great majority this seasonal predominance exists.

During these seasons there is a greater variability of the meteorological environment. Thus it would appear that this factor must play an important rôle in the reaction of the unstable individual who is afflicted with an ulcer.

In this connection the report of Preuner¹ on the effect of weather conditions on experimental asthma in guinea pigs is interesting. He found in a statistical study that the induced asthma was not dependent on such meteorological factors as temperature, humidity or atmospheric pressure as long as these factors remained constant, but that during periods of rapid change in weather conditions the average severity could be increased about 50 per cent. The fact that these meteorological

factors are thus subject to accurate statistical study in laboratory animals is of basic scientific interest and, as pointed out in the *Journal of the American Medical Association*,<sup>2</sup> the new field of experimental meteorobiology may conceivably assume an important rôle in future therapeutic study.

Clinically, other diseases and symptom complexes exhibiting periodicity are those of the skin, prostate, certain types of asthma and hay fever, sinusitis and the historical shoemakers' tetany. Pulmonary emboli as Peterson and deTakats have shown, are predominantly seasonal in their occurrence. There are also seasonal variations in the calcium, phosphorus and vitamin C levels of the blood. The iodine content of the thyroid gland in animals has been shown to vary markedly with the seasons, as recently brought out by Fenger. These are a few examples demonstrating the seasonal tide.

Experimentally, ulcers have been produced in the stomachs of dogs by the use of pitressin, in the exact location as seen clinically in man. The blood supply to the tissue was diminished through increased tone or actual spasm of both muscle and blood vessels, with subsequent digestion of the involved area producing an ulcer. Time does not permit further examples.

From these facts it can be seen that we are not dealing with an organism that is static and immutable but with an integrated and highly complex mechanism which must adjust itself continuously to the forces in its environment, both external and internal. Meteorological forces such as changes in temperature, humidity, barometric pressure and the intensity of light are the most constant to which the individual must adjust himself.

Dietetic factors such as lack of intake or loss of certain vitamins or minerals play an important part.

It is not reasonable to assume that a constitutionally unstable individual who may be depleted of certain substances or

<sup>&</sup>lt;sup>1</sup> Preuner, R. Allergiestudien. Ztschr. f. Hyg. u. Infektionskr., 1939, 121, 559–568.

<sup>&</sup>lt;sup>2</sup> Current Comment. J. Am. M. Ass., 1939, 113, 1036.

changed chemically by other factors is going to react emotionally in the same way as another individual who is well buffered in his chemical and constitutional makeup. However, let us not forget the tremendous rôle that emotional disturbances can play producing both psychic and physical disturbances.

I have attempted to present some of the environmental factors which affect the individual, and have brought to your attention two conditions which seem to be local expressions of a system disturbance. The first, a spasm, expressing itself as a dysfunction, and the second, an ulcer, which goes through the stage of dysfunction on to tissue death and digestion.

Fundamentally it would appear that pylorospasm is the result of an autonomic imbalance and that ulcer is an expression of an oxygen lack brought on by diverse environmental factors, both internal and external, in a constitutionally inadequate individual.\*

\* For discussion see page 841.



tained by him from a study of 69 nurses and laboratory workers; the leukocyte count here varied between 3,500 and 7,500 and the percentage of lymphocytes between 20 and 50; also here a leukopenia was obtained in 50.5 per cent. In these cases the lowest leukocyte count was 3,500 and the highest lymphocyte percentage was 50.5.

Especially interesting were the results obtained by the same author in the course of the last twelve years from a study of 344 physicians, nurses and technicians of the Holfelder Roentgen Institute. The leukocyte count in these cases varied between 4,000 and 8,500 and the lymphocyte value between 20 and 45 per cent. A leukopenia was found in 46 per cent of the cases. The lowest leukocyte count obtained was 3,500 and the highest lymphocyte value was 57.5 per cent.

Gansslen definitely demonstrated the climatic and geographic influences on the white blood picture. These observatoins clearly show that the leukocyte and lymphocyte values in the healthy individual are subject to greater variations than hitherto assumed. Slight quantitative changes in the white blood picture appear, therefore, not as pathologic but as physiologic reactions. They may be explained by the dynamics of the blood regulation dependent on the vegetative nervous system which in its turn is intimately related to the hormones. The important recognition of the normal variations in the white blood picture are essential for the evaluation of blood injuries observed in the personnel associated with roentgen rays. This author is of the opinion that a leukocyte count of 3,500 and a lymphocytosis up to 60 per cent observed in a radiologist or a roentgen technician should no longer be looked upon as pathologic. Also the quantitative deviations of a slight degree found in the remaining blood picture should not be looked upon as roentgen injuries but should be considered as due to vegetative nervous reactions which have nothing to do with the radiation effect and which are not pathologic. However, if the leukocyte count is below 3,500 and the lymphocyte value exceeds 60 per cent, the findings should be considered as pathologic and if observed in radiologists or roentgen technicians should be related to the effect of roentgen rays. If the above are found in association with a pronounced shift to the left in the white blood picture as well as the presence of individual myelocytes and myeloblasts, then the findings point clearly to a radiation injury. Findings of the last mentioned type are usually associated with changes in the red blood picture expressed in the form of anisocytosis, poikilocytosis, polychromasia and an increased number of reticulocytes as well as of the normoblasts.—A. S. Schwartzman.

BAUER, R. Zur Kenntnis der Strahlenschädigung der menschlichen Lunge. (Contribution to our knowledge of radiation injury of the human lung.) *Strahlentherapie*, 1939, 64, 249–266.

The author reports a case of roentgen injury to the lung which led to death, which he discusses from the clinical-roentgenologic viewpoint. A mediastinal tumor which extended in the left upper field, in all probability a thymogenic carcinoma, was given three series of roentgen treatments. The author reports exactly and in detail the course of the disease, the size of the dose and the time of irradiation. The autopsy revealed besides the extensive radiation induration of the lungs which led to death, also a large indurated body in the upper mediastinum in which tumor cells were no longer demonstrable.

In his report the author discusses extensively the literature dealing with the subject and the conditions under which such severe radiation injuries to the lung may occur. Besides the size of the roentgen dose and the intervals between the irradiation other conditions also, especially inflammatory processes in the lungs, favor the development of the radiation injury. A special predisposition to an inflammatory connective tissue reaction of the lung peculiar to a given individual may play an important rôle. In consideration of the fact that because of the anatomical structure of the thorax the actual percentage of the deep radiation dose cannot be determined with absolute certainty, excessive care is recommended in roentgen irradiation of the thorax.—A. S. Schwartzman.

Schairer, E., and Krombach, E. Röntgenstrahlenschädigung der Lunge mit tödlichem Ausgang. (Roentgen injury of the lung with fatal termination.) *Strahlentherapie*, 1939, 64, 267–290.

A woman, aged thirty-nine, was subjected to intensive roentgen irradiation because of a mediastinal tumor; under the influence of this irradiation there occurred a complete indurative transformation of the tumor and a destruction of all tumor cells.

Death of the patient occurred as a result of a pulmonary injury produced by the roentgen rays.

An attempt was made by the authors to delimit the picture of pulmonary injury resulting from roentgen rays on the basis of their personal observations and on the basis of the cases reported in the literature. Attention is called to the fact that besides the latent period two stages must be principally differentiated: the main reaction with the more or less acute inflammatory processes and the stage of regression with connective tissue proliferation. In men, however, these two stages cannot be as distinctly differentiated because of the prolongation or spread of the radiation.

The pathogenesis of the pulmonary changes is considered by these authors on the basis of Richer's vascular theory. By the aid of this theory the differences in the pathologico-anatomical and clinical findings obtained by the various authors may be easily explained.

These authors do not accept the designation of Desjardins' "roentgen pleuropneumonitis" applied to this type of pulmonary injury. These authors prefer the designation of "acute or chronic pneumonia resulting from roentgen irradiation."—A. S. Schwartzman.

Buhtz, Helmut. Über Schädigung des Darmes bei Röntgenbestrahlung. (Injury to the intestines by roentgen rays.) *Strahlentherapie*, 1939, 64, 291–310.

The author reports the history, clinical course and autopsy findings of 3 cases of injury to the intestines by roentgen rays. Macroscopially in all these cases there developed a pronounced ulcer formation in the intestines. The histologic examination revealed necrosis of the intestinal wall of a variable degree, in some cases leading to a complete wall defect with fibrosis of the submucosa and occasionally hyperplasia of the muscularis, injury to the serosa, slight infiltrations of a chronic inflammatory type and especially vascular changes in the form of slight endarteritis and in some cases a total endophlebitis obliterans. These intestinal injuries were found also in the neighboring macroscopically appearing intact, intestinal regions.

For the verification of the diagnosis of roentgen injury the findings were compared with similar findings in the intestine in other diseases such as tuberculosis, dysentery, intestinal lues, uremia, endemic sprue, coprostasis and lymphogranulomatosis. The author also compares the histologic findings made in his cases with those reported in the literature and discusses the topographic localization of the injuries which he relates with the peculiarities of the radiation process.

The author discusses cases of a similar nature reported in the literature and considers the causes which may lead to a roentgen injury of the intestine; he considers in detail the physical properties of roentgen radiation and the possibility of a combination injury based on conditions such as peculiarity of the tissues resulting from predisposing factors or from some vascular injuries which have influenced the end-results of the roentgen rays; he also considers the general biological effect of roentgen rays.—A. S. Schwartzman.

Chaoul, H. Bisherige Ergebnisse der Röntgennahbestrahlung freigelegter Rektumkarzinome. (Results hitherto obtained in the treatment by close roentgen irradiation of exposed carcinoma of the rectum.) Strahlentherapie, 1939, 64, 219–226.

In a previous communication the author reported the results obtained in the treatment of 8 patients suffering from inoperable carcinoma in which a disappearance of symptoms was obtained following an exposure of the carcinoma and a close roentgen irradiation. This method is essentially a combination of surgical and roentgen treatment. The surgical treatment consists in the direct exposure of the tumor so that it can be reached by the rays similarly to a superficially situated tumor. The surgery consists basically, therefore, in a resection of the coccyx and lower segment of the sacrum after which the rectum is mobilized, split and its two borders are fixed into the skin wound by sutures. The tumor exposed in this manner is then subjected to roentgen irradiation. The diseased region is irradiated daily with doses varying from 150 to 5∞ r. The irradiation is continued until the tumor has disappeared completely. To achieve this, in the author's practice, a total dose of 12,000 to 15,000 r was found necessary. The author emphasizes the absolute necessity, in treatment of this type, of fractionating the dose since this, he believes, makes possible the sterilization of the carcinoma cells. As a rule towards the end of the treatment there occurs a reaction of the mucosa manifested in the form of a deposit on the irradiated region of the intestinal mucosa. The duration of this phenomenon lasts from six to eight weeks and in unusual cases it may last even a few months. Occasionally also the intestinal wall reacts in the form of a sclerosing edema which may eventually require surgical treatment.

•Employing this method 23 patients, practically all of which had inoperable carcinoma of the rectum, were treated.

In 14 of these a complete disappearance of the tumor was obtained. Two of these patients were under observation for about four years, I for three years, 3 for two years and the remainder for over one year. In all the successfully treated patients a gain in weight of 20 to 40 pounds was obtained. In all the cases which were subjected to a restorative surgical operation following the disappearance of the tumor a normal intestinal function was obtained. In consideration of the hopelessness of cases of this type the author considers the results presented above as satisfactory.—A. S. Schwartzman.

Walther, O. Resultate der Strahlenbehandlung bei Sarkomen. (Results of radiation treatment in sarcoma.) Strahlentherapie, 1939, 64, 59–112.

Between 1919 and the end of 1936, 240 cases of sarcoma were treated and followed up in the Roentgen Institute of Zurich; 132 of the cases were males and 108 females and the average age of the patients was 44.8 years. In this number cases of solitary giant cell tumor, cases of lympho-epithelial tumor and melanoma were not included. The distribution of the sarcoma in the cases studied was as follows: 19 per cent along the digestive tract, 16 per cent along the supporting tissues with the exception of the bony system, 14 per cent in the bony system, 13 per cent in the region of the respiratory tract, 12 per cent in the region of the thyroid gland, 9 per cent in the region of the lymph node system, 7 per cent in the region of the genitourinary tract and 2 per cent in the mammary glands. In 91 per cent, or 219 cases, the diagnosis was verified histologically and was as follows: round cell sarcoma in 37 cases, lymphadenoid sarcoma in 36 cases, spindle cell sarcoma in 32 cases, polymorphocellular sarcoma in 27 cases, sarcoma without more distinct differentiation in 26 cases, fibrosarcoma in 14 cases, hemangio-endothelioma in 12 cases, Ewing's sarcoma in 10 cases, reticulo-endothelial sarcoma in 9 cases, osteogenic sarcoma in 6 cases, myxofibrosarcoma in 5 cases, plasmocytoma in 4 cases and myeloma

in one case. In 9 per cent, or 21 cases, no histological verification was obtained.

Of the 240 cases, 38, or 16 per cent, were treated surgically-radiotherapeutically and 202, or 84 per cent, were treated exclusively by radiation therapy. In 145 of the 202 cases, or 72 per cent, at attempt was made to obtain a cure by radiation therapy and in 57 patients, or 28 per cent, the irradiation was given for palliative purposes purely, since a cure could no longer be expected.

Two hundred thirty-seven of the 240 cases have been followed up in the course of one year after the treatment. Of these 69, or 29 per cent, were free of symptoms; 223 cases were followed three years after the treatment and of these 44, or 20 per cent, were found free of symptoms, while 201 cases were followed five years after the treatment was terminated and of these only 26, or 13 per cent, were free of symptoms.

Of the 240 cases only 31, or 13 per cent, were in an operable stage at the time radiation therapy was instituted, while 209, or 87 per cent, were in the inoperable stage. The results obtained in the operable cases were as follows:

Nineteen of the 31 cases, or 63 per cent, were free of symptoms after one year; 14 cases, or 56 per cent, were free of symptoms after three years and 7 cases, or 35 per cent, were free of symptoms after five years. Of these 31 cases only 1, a bilateral round cell sarcoma of the mammary gland, was locally cured by the exclusive use of radiotherapy but died from a generalized metastasis. The remaining 30 cases were first operated on and then given radium therapy.

Two hundred five of the 209 inoperable cases could be followed up and the results obtained were as follows:

Forty-eight of the 205 cases, or 23 per cent, were free of symptoms after one year; 29, or 14 per cent, were free of symptoms after three years, and only 10 per cent were free of symptoms after five years.

The best results, judged on the basis of a five year follow up study, were obtained in cases of tumors of the eye region, ear region, mouth cavity, mesopharynx, mediastinum and the supporting structures of the body. The permanent cures here exceeded 25 per cent. In other localizations either slight or no permanent cures were obtained.

One hundred eighty-one of the 240 cases of sarcoma, or 75 per cent, died as a result of the disease; 113 of these, or 62 per cent, were favor-

ably influenced palliatively. The average duration of life of the patients who died following irradiation from neoplasms was \$12.2 months. Good palliative results were obtained in tumors of the accessory nasal cavities, of the epipharynx, mesopharynx and of the mediastinum. Poor palliative results were obtained in tumors of the kidneys, colon and urinary bladder.—A. S. Schwartzman.

Mayer, A. 30 jahrige Erfahrungen über Uteruskarzinom-Therapie. (Experience of thirty years with therapy of uterine carcinoma.) *Strahlentherapie*, 1938, 63, 407–413.

The curative results in cases of uterine carcinoma obtained in various clinics vary considerably and are therefore not always comparable. In consideration of the above it appears desirable to discuss the results obtained in the treatment of uterine carcinoma in the course of the last twenty years by the author and the results obtained by Döderlein in the course of ten years which were followed up by the author.

The methods of treatment employed during these years were as follows: pure surgical, surgery combined with prophylactic after-irradiation, preliminary irradiation followed by surgery and pure irradiation.

The present report, therefore, deals with the results obtained from these various methods. Altogether 1,900 cases of carcinoma of the cervix were treated. The criterion of the results obtained was based on the absolute permanent cure, the surgical mortality and the working ability of the patients in inoperable cases. An absolute permanent cure of the cases observed was obtained in about 20 per cent and a relative cure in the surviving operated patients was obtained in 39.3 per cent. The primary surgical mortality varied between 18 and 20 per cent.

An attempt was made to improve the surgical permanent cure and therefore surgery was complemented by prophylactic after-irradiation. In 85 cases where this method of treatment was employed the relative cure of 39.3 per cent was increased to 47 per cent. Next an attempt was made to decrease the primary surgical mortality. In nearly 50 per cent of the cases death was due to peritonitis. To eliminate this a prophylactic preliminary irradiation was carried out. In 91 cases where this treatment was used the total postoperative mortality was

only 4.5 per cent and the mortality due to peritonitis proper was only 1.1 per cent.

Eventually the radium-roentgen treatment was basically employed. For purposes of evaluation of the results obtained, 147 cases were available with an operability of 48 per cent. The relative cure obtained in these cases was 46.9 per cent in comparison with the 47 per cent obtained from surgery. Otherwise, however, irradiation was found preferable to surgery, since the irradiation has practically no primary mortality, and is employable in each case including the inoperable cases. Irradiation also gives a better absolute cure, namely, 30 per cent in comparison with 20 per cent obtained from surgery and a relative cure of 17.4 per cent in the inoperable cases. The data presented above clearly show the full justification of radiation treatment of carinoma of the uterus. It is not only not inferior to surgery, but in some respects actually superior.

The operability of carcinoma of the body of the uterus as judged on a study of 450 cases was found to be equal to about 80 per cent. The postoperative mortality in these cases was 9.6 per cent. The absolute cure obtained in all the observed cases was 46 per cent. With the addition of the prophylactic after-irradiation employed on 124 cases, an absolute cure of 48 per cent was obtained. A relative cure of the operative cases was obtained in about 60 per cent, and was therefore considerably higher than in cases of carcinoma of the cervix. Contrary to the results obtained from surgical treatment by means of pure irradiation, an absolute cure was obtained in only 33 per cent, therefore inferior results to those obtained from surgery. In consideration of the results obtained this author recommends and actually employs surgery as a rule in cases of carcinoma of the body of the uterus and only exceptionally uses irradiation. The following conclusions are drawn by the author:

Roentgen-radium irradiation is the usual method of treatment in carcinoma of the cervix. Surgery must be considered in carcinoma of the uterus, in rare cases of carcinoma of the cervix during pregnancy in carcinoma of the cervical os or the so-called central carcinoma nodules which are frequently the adenocarcinoma type, and in carcinoma of the cervix of young women which appears especially malignant. As a second choice surgery is considered in carcinoma of the cervix refractory to roentgen rays which do not respond sufficiently six to

eight weeks after the irradiation, in cases where an apparent cure has been obtained from irradiation but where a bloody, foul smelling discharge persists pointing to a carcinoma in the deeper regions, in the rare cases of radiogenic vaginal stenosis where a bloody or foul smelling discharge points to carcinoma in the deeper regions and in the occasional operable carcinoma recurrences following irradiation.—

A. S. Schwartzman.

Schmiemann, Rolf. Ergebnisse der Strahlenbehandlung des Uteruskarzinoms an der Würzburger Universitäts-Frauenklinik. (The results of radiation treatment of carcinoma of the uterus at the Würzburg University Women's Clinic.) Strahlentherapie, 1938, 63, 583–613.

The author reports the results obtained in the course of nine and a half years, from January 1, 1924 to July 1, 1933, from pure radiation treatment of uterine carcinoma employed in the Würzburg University Women's Clinic. The treatment consisted always in a combined application of roentgen and radium rays. The report of the results is based on the accepted standards for statistics dealing with carcinoma as suggested by Winter and Voltz. Special attention has been paid not only to the data dealing with restoration of efficiency or cures, but also to the mortality and to the duration of life of the irradiated carcinoma patients. A classification according to age revealed a clear cut predominance of the fifth decade over all other age groups. No difference could be obtained regarding the results from irradiation as related to different age groups.

A comparison of the results obtained in different clinics from radiation therapy and surgical treatment in uterine carcinoma, as reported in the literature, revealed a definite superiority of the results obtained in the treatment of carcinoma of the uterine cervix in the University Clinic of Würzburg, in comparison with the results obtained in other clinics from pure radiation treatment or pure surgical treatment. No such clear cut superiority could be demonstrated in regard to the results obtained from the treatment of carcinoma of the uterus. Even though a definite answer to the question whether radiation treatment or surgery should be employed in carcinoma of the uterus cannot be given, nevertheless, in consideration of the developmental possibilities of radiation therapy, in comparison with the possibilities of surgery which has practically already reached its peak, the author is inclined to state that he believes in the great future of pure radiation therapy.—A. S. Schwartzman.

CAFFIER, P. Ergebnisse und Erfahrungen der Kollumkarzinombehandlung mit besonderer Berücksichtigung der Radiumtherapie. (Results and experiences in the treatment of carcinoma of the cervix with special consideration of radium therapy.) Strahlentherapie, 1938, 63, 639-657.

The report deals with the results and experiences of Stoeckel's clinic in Berlin in the "selective" treatment of carcinoma of the cervix and the results are based on a study of seven years' duration. Of the 1,314 cases of carcinoma of the cervix treated during this time, an absolute cure was obtained in 28.9 per cent. A relative cure obtained by operation was demonstrated in 45.9 per cent (399 cases) and a relative cure obtained by irradiation was demonstrated in 21.9 per cent. The author discusses in detail the technique of the radium treatment of carcinoma of the cervix routinely employed in Stoeckel's clinic. The relative irradiation of the early cases of carcinoma (Groups I and II) was 35.8 per cent and was, therefore about 10 per cent below the cures obtained by operation, which points to the preferability of surgery. The efficiency of radiation therapy is especially imposing in the poor cases in which it still offers a permanent cure in about 13.2 per cent of the cases. The pure primary radium mortality was 1.5 per cent in the 905 cases treated in this manner, the infection mortality was only 0.7 per cent. The irradiation injuries referable to radium under the technique employed were demonstrable in only 3 cases in the form of an ulcerative proctitis.—A. S. Schwartzman.

Wasserburger, K., and Smereker, H. Die Radiumbehandlung des Gebärmutterhalskrebses. (The radium treatment of carcinoma of the uterine cervix.) *Strahlentherapie*, 1938, 62, 584–600.

An attempt was made by the authors to determine the dosage distribution in radium therapy of carcinoma of the uterine cervix. This study was referred chiefly to the methods of treatment employed in the Radiological In-

stitute of Vienna in the form recommended by Forssell and Heyman, on one hand, and by Regaud, on the other hand. The dose measurements were carried out according to the condenser chamber methods of Sievert and the doses were reported in roentgens and in imc. h. In order to determine the dose which actually acts on the tumor the measurements were carried out in the immediate proximity of the applied radium preparation. The study of the distribution of this dose of rays on the greatest path of extension of carcinoma of the uterine cervix such as the parametrial tissue, the urinary bladder, rectum and the lymph nodes was carried out on preparations of cadavers. The results obtained from the dose measurements were compared with the clinical experience from the use of the radium therapy in the treatment of carcinoma of the uterine cervix. It was found during these studies that in order to prevent a pronounced change of the mucosa in either of the two methods referred to above, a new packing of the vaginal radium applicator is necessary. It was further found that in advanced cases of carcinoma of the uterine cervix a carefully planned roentgen irradiation following the radium application is necessary.— A. S. Schwartzman.

Pickhan, A. Die intrauterine Radiumbehandlung der hämorrhagischen Metropathien. (The intrauterine radium treatment of hemorrhagic metropathy.) Strahlentherapie, 1938, 63, 682–688.

A new period of special research and treatment of diseases dependent on animal germinal glands has been instituted with the discovery of the high radiosensitivity of these animal germinal glands. Especially the recognition of the relation of the so-called benign uterine affections with the disturbance in the ovarian activity led to the development of a procedure which at present may be looked upon as the method of choice in the treatment of these affections. There exists a large group of uterine hemorrhages which are not of a malignant origin but which frequently lead to conditions dangerous to the life of the patient, in which modern radiation therapy assumes a dominant position. Reference is had here to the hemorrhagic metropathia, especially the climateric and preclimateric hemorrhages the cause of which must be looked for in pure functional disturbances in the ovarian inner secretory activity.

The ovaries are glandular organs, the cells of which are in a constant state of development. With the progress of proliferation the radiosensitivity of the follicular apparatus increases. In the resting mature follicles the radiosensitivity is decreased. Two paths are accessible to therapy, namely a uniform destruction of all ovarian cells and a partial elimination of function of the most sensitive part of the follicular apparatus. Both these purposes can be achieved by deep roentgen therapy.

This author employs weakly filtered radium radiation in cases of hemorrhagic metropathies. This treatment is employed preferably in individuals of the preclimateric age. In all other cases of hemorrhagic metropathy of a benign cause, roentgen therapy is employed when no surgical indication exists. In regard to treatment, the author emphasizes the importance of a thorough history, with special attention to previous infectious diseases of the genital organs or their appendages. The treatment can not be employed in cases of recent inflammatory processes of the genital organs. In cases where there is a previous history of adnexal diseases, a careful control of the temperature of the patient is necessary. A thorough blood picture must be obtained. In each case an exploratory curettage must precede the treatment in order to exclude malignancy. The patient is prepared for the treatment in the course of two to three days after admission and this preparation consists in antiseptic treatment of the vagina, cervix and cervical canal by means of tampons soaked in antiseptic solution. The amount of radium employed is determined by the size of the uterine cavity. In most cases 30 to 50 mg. of radium is necessary and the radium is introduced under aseptic precautions. The average dose is about 1,500 mg. hr. The average age of the women treated in this manner is 43.3 years and in each case permanent amenorrhea is obtained on the average after 0.7 months.

Not in a single case did this method of treatment prove ineffective. Not in a single case were any undesirable side effects observed. Following each treatment, however, the patients should be under observation; especially during the first months after the treatment an occasional sounding of the uterine cavity is necessary in order to prevent any possible occlusions of the cervical canal and a consequent infection.

This type of treatment must not be employed in women suffering from chronic inflammatory

processes of the adnexa as well as in all cases with acute or chronic processes of the genitals. It must be remembered that in cases of the last mentioned type also percutaneous radium therapy is not without danger.

It is surprising how soon after the radium treatment the general condition of the patient improves and the patient is in a position to return to work. The author believes, on the basis of his experience, that intrauterine weakly filtered radium therapy is the method of choice in the treatment of preclimateric hemorrhages.

—A. S. Schwartzman.

Crainz, Franco. Die Behandlungserfolge bei den bösartigen Eierstocksgeschwülsten. (The results obtained in the treatment of malignant tumors of the ovaries.) *Strahlentherapie*, 1938, 63, 434–464.

- 1. Each case of a malignant tumor of the ovaries must at first be operated on; if a complete surgical removal of the tumor is impossible, as much of the tumor as possible should be removed.
- 2. In cases where the tumor is present only on one side, the second ovary, which may be perfectly healthy, must also be thoroughly removed. The uterus should be left intact.
- 3. In each case radiation therapy should be given after the operation even when the entire tumor has apparently been removed. As much as possible it should be given in the form of a homogeneous roentgen irradiation of the pelvis and lower abdomen and an additional intrauterine radium application should be carried out.
- 4. In those cases where no surgery can possibly be carried out, irradiation should be employed if the general condition of the patient permits it. Also in cases of this type a combined roentgen-radium irradiation is desirable.
- 5. The results obtained from the treatment carried out according to the above given method in the University Clinic of Würzburg are better than any hitherto reported in the literature. Of the 152 patients with malignant tumors of the ovaries observed, 23.7 per cent were still alive after five years; of the 131 treated cases, 27.5 per cent were still alive after five years. Of the 38 cases where the tumor was thoroughly removed surgically, 60.5 per cent were still alive after five years. Of the inoperable cases (incompletely surgically removed tumors and postoperatively irradiated or exploratory laparotomies and postoperatively ir-

radiated or only irradiated cases), 14 per cent were still alive after five years; of the inoperable cases, 19.5 per cent were alive after five years of those where the tumor was partly removed while only 4.5 per cent of the cases remained alive after five years where the exploratory laparotomy was followed by irradiation; of those inoperable cases which were treated only by irradiation, 13.3 per cent were still alive after five years. Of all surgically treated carcinoma cases 25 per cent were alive after five years and of all the surgically treated sarcoma cases 100 per cent were still alive after five years.

6. The therapeutic results presented above are of especial value because they were obtained from a definite plan of treatment, because the results are classified on the basis of the different types of treatment and because the percentage of cases after five years' observation was determined.—A. S. Schwartzman.

#### MISCELLANEOUS

Crowther, J. A. Die biologische Wirkung der Röntgenstrahlen. (The biologic effect of roentgen rays.) *Strahlentherapie*, 1938, 62, 569–583.

Experimental studies of the biologic effect of roentgen rays have been carried out since 1895. The literature dealing with this subject is extremely extensive. A study of this literature reveals that best results were obtained when the effects of roentgen rays were studied on simple systems. This author also limits himself to the study of the effect of roentgen rays on individual cells and unicellular organisms. Experiments of this type show an unusual variability of the radiation effect on different types of tissues. For instance, even a dose of 40 r may kill about 50 per cent of some unicellular organisms; on the other hand, a dose of 330,000 r is necessary in order to produce death of 50 per cent of the individuals of a Colpidium culture. An elimination of cell division may be obtained in tissue cultures with a dose as small as 120 r; on the other hand, a dose of 13,000 r is necessary in order to achieve a complete death of the cells. During cellular division the cells are more sensitive to roentgen rays, and rapidly growing non-differentiated cells are in general more sensitive than mature cells. Doses of roentgen rays capable of killing all types of living tissue are beyond 100,000 r. This effect, which is nonspecific, is no doubt based on chemical changes

in the cytoplasm produced by the changes in the tissues. Photochemical changes are demonstrable in many types of organic and inorganic substances when large doses of roentgen rays are used. The effect is chemically demonstrable following the use of a dose of 2,000 r, a dose, therefore, 50 times as strong is necessary in order to change the cellular cytoplasm to such an extent that it would produce death of the cell. It is not surprising, therefore, that a tissue culture may be led to death from the use of a dose of 100,000 r. On the other hand, it is quite surprising that in the same tissue only 1/1000th of this dose is capable of producing extensive biological effects.

The effect of some roentgen-ray doses may be classified in three groups: (1) elimination of the division ability of the cells; (2) production of mutations, and (3) in certain cases, especially in cells which divide rapidly, death.

Mitosis and mutations are functions of the cellular nucleus. The destruction in the rapidly growing tissues is probably conditioned by the inability of the irradiated cells to divide. In all probability, therefore, in each case the radiation effect does not involve the cell as a whole, but especially the cellular nucleus. Vitemberger demonstrated experimentally that in a resting stage the cellular nucleus is 25 times as sensitive to roentgen rays as the cytoplasm.

Experimental studies further justify the statement that the point of the radiation effect is not limited to the nucleus as a whole but to certain structures of the nucleus. The resting nucleus appears completely homogeneous. By means of the usual microscopic methods not a trace of the structural richness of the nucleus is demonstrable. According to the general view of cytologists the apparent uniformity of the nucleus actually exists. During this stage the cell is relatively slightly sensitive to roentgen rays. With the appearance of mitosis the characteristic cell division structures appear and especially during this stage of the life of the cell it is very sensitive even to small roentgenray doses. The appearance of cell division structures and the increased sensitiveness are doubtless not accidental in nature. Still more conclusive proof is obtained from experiments dealing with the radiation effect on the hereditary mass. An effect of this type cannot be reproduced to the same degree by any other agent. The gene theory of mutations is one of the best founded biological theories and each radiation effect must in the last analysis represent an effect on a gene. In this manner, the specific effectiveness of the roentgen rays on particles of submicroscopic dimensions is conclusively proved.

The relationships between the dose and biological effect have been very thoroughly studied. The results of these studies are usually represented in the form of curves which illustrate the percentage of the surviving individuals dependent on the radiation dose.

The explanations of the biological mode of action of roentgen rays may be classed into two main groups which may be briefly designated as the toxin and the "hitting" theories. According to the toxin hypothesis, the radiation produces as a result of a photochemical influence of the nuclear substance a nonspecific toxically acting substance which by way of diffusion into the neighboring tissue leads to the observable changes.

According to the "hitting" theory the effect of roentgen rays comes to manifestation when a sensitive biological structure is hit by the roentgen rays. Both theories are rather well substantiated. This author is of the opinion that basically the biologic effect of roentgen rays is to be explained by the changes in the electric charge proper. The appearance of the different structures at the beginning of mitosis is highly similar to the coagulation of colloid particles and it is known that the structures are electrically charged. The equilibrium between the differentiated and homogeneous phases of the nucleus must be very labile so that at a critical point a change in the charge is easily achieved and this change disturbs the entire course of the mitosis or disturbs the normal distribution of genes and thereby leads to a mutation. A few years ago this author, together with Fairbrother, showed that positively charged colloids may be destroyed by roentgen rays. The dose necessary for this purpose is relatively large but the colloids employed in these experiments were more distant from the isoelectric point than those occurring in the biological material. Recently this author, together with Liebmann, discovered the fact that even with a dose of roentgen rays as small as 20 r the electrokinetic potential can be changed by about 10 per cent. Changes of the potential of the colloid of a similar degree may produce definite biologic effects in the cellular nucleus. -A. S. Schwartzman.

Daels, Franz, Fajerman, H., and Wande-Putte-van Hove, W. Wie sich beim Versuchstier eingespritztes lösliches Radium in den verschiedenen Körpergeweben verteilt. (The distribution of soluble radium in the various body tissues following its injection into the experimental animal.) Strahlentheravie, 1938, 63, 545-555.

A series of experiments was carried out by the authors of the following nature: A white rat. inoculated with a sarcoma tumor of about 1.5 cm. in diameter, during an advanced state of pregnancy, was given subcutaneously daily in the course of three days in succession I cc. of a radium solution of 1:400,000, that is, 0.0075 mg. of radium. The animal was killed six hours after the last injection and many sections from various tissues were made for imbedding and drying. The following dried tissue when acting on a film in the course of seven days rendered the film black: bone, liver, kidney, fetus and skin region where the injection was made. After four weeks also blood and lung tissue rendered the film black. The appearance of the film was doubtful under the influence of spleen, placenta, amniotic fluid and stomach tissue. No effect whatsoever was obtained from sarcoma tissue, heart, suprarenal tissue, brain and muscle tissue. The imbedded tissue gave a weaker effect apparently as a result of the washing which preceded the imbedding. The tissues which, according to these experiments contained most radium, were bone, liver, kidney and fetus. The placenta, therefore, did not act as a storing organ and the tissue of the fetus retained more radium than the placenta.

In another experiment a pregnant guinea pig inoculated with sarcoma tissue was given some radium injection shortly before delivery, receiving altogether 0.02 mg. of radium. Seven hours after the last injection the guinea pig was killed. Also in this experiment the liver, kidneys and lungs were found to contain radium; also here the placenta and fetus contained radium and also here the placenta did not prevent the penetration of radium into the fetus. Numerous other experiments were carried out by these authors and the following results were obtained:

Pregnant and non-pregnant mice, white rats and guinea pigs were given soluble radium as well as various animals inoculated with sarcoma tumors. For purposes of demonstration of the radium in the tissues the roentgeno-

graphic picture was utilized. The films were subjected to the influence of the various organs in the course of one week up to three months. These studies have shown that the radium was found in largest amounts in the organs which are considered as excretory organs such as liver, kidneys and lungs, as well as in those which function as blood forming tissues, such as bony tissue, liver and spleen. The placenta and fetus both contained some radium and the placenta did not prevent the penetration of radium into the fetus. Sarcoma tissue does not contain excessive amounts of radium. Only traces and in • some cases no radium was found in the muscle and brain tissue. The largest amount of radium was found in the bony tissue; relatively large amounts of radium were found in the liver and spleen and somewhat later also in the kidneys, intestines and lungs. Small amounts of radium are found in the sarcoma tissue and in the blood only during the first three days following the last radium injection.—A. S. Schwartzman.

Reding, R. Über den Einfluss von Eiweissabbauprodukten auf die Vorgänge bei der Krebsbildung. (The influence of protein decomposition products on the processes in carcinoma formation.) Strahlentherapie, 1938, 63, 556–560.

It is generally assumed that two essential factors must cooperate in order to make possible the appearance of carcinoma, namely, the local factor: a cellular decomposition and regeneration focus, and the general factor: the predisposition. Below the author discusses the significance of protein bodies for the appearance of these two factors. Recent studies have substantiated the old observation that cellular destruction and regeneration precede the development of a carcinoma. It is at present an accepted fact that cellular dissolution foci and proliferation foci which correspond to the chronic ulcer formations may occur within the tissue frequently without actually producing a genuine ulceration. Under these conditions they represent the closed cellular dissolution and proliferation foci. In the mammary gland, for instance, there occurs under the influence of estrin an alternation between necrosis and proliferation. Similar conditions are found in indol poisoning in the bone marrow, in some parenchymatous organs under the influence of protein bodies and in the reticulo-endothelial system under the influence of tar. The various

carcinoma producing substances which differ vitally in their nature have, therefore, the same biological effect; that is, produce within the tissues latent foci of cellular dissolution and proliferation the effect of which is identical with chronic ulcerations. The similarity of the latent chronic cellular dissolution foci with chronic ulcerations permits a uniform definition of all carcinoma producing substances and enables the explanation of the localization of many deeply situated forms of carcinoma. In the local focus the protein bodies which origi-. nate during the cellular dissolution lead to the development of cellular proliferation. On the other hand, the absorption of protein decomposition products which reach into the circulation during the cellular dissolution leads to a definite intoxication of the body which represents the cause of the predisposition to carcinoma.

The predisposition to carcinoma implies the existence of relations which predispose and promote the appearance, propagation and the development of the peculiar metabolism of malignant cells. The following are the conditions which determine this predisposition: (1) Humoral changes, such as an alkalosis, an increased content in polypeptids, aminoacids, fibrinogens, globulins and cholesterin. (2) Functional disturbances; a diminished oxygen supply to the tissue, an increased glycolysis, disturbances in the blood sugar regulation, a paralysis of the reticulo-endothelial system, an increased water content of the tissue and a vagotonia. (3) Endocrine disturbances; hypertrophy of the anterior lobe of the hypophysis

and a certain increase in the number and volume of the islands of Langerhans.

The pathogenesis of the general carcinoma predisposition seems, therefore, to consist of an intoxication of the body with protein decomposition products. These protein decomposition products are endogenous or exogenous in origin, depending on the fact whether they are derived from the body proper or from exogenous protein bodies. The exogenous intoxication occurs as a rule through the food intake. It has been proved that complex polypeptids may reach the peripheral circulation when the protein utilization by the liver is insufficient. An acute protein intoxication, digestive in nature, may appear as a result of intestinal obstruction which is followed by an excessive absorption. A chronic protein intoxication may occur in individuals who superficially appear healthy but who suffer from a liver insufficiency especially affecting the protein metabolism.

The work is concluded with the statement that the closed foci of cellular dissolution and regeneration are the analogies of chronic ulcers and with the statement that the humoral pathologico-anatomical and functional symptomatology of the carcinoma patients is not specific; similarly it is not irrelevant or secondary because it seems to present signs of a protein intoxication. The fact that many humoral changes appear exactly identical in carcinoma patients and in various other protein intoxications explains the fact why hitherto specific humoral changes have not been demonstrated in carcinoma patients.—A. S. Schwartzman.



proctosigmoidoscopic findings are lacking. Frequently, however, roentgenologic and proctosigmoidoscopic diagnoses are found to be in disagreement, and now and then the evidence yielded by one or the other or by both examinations is such that a definite diagnosis is not forthcoming. It is in such instances that the clinician finds that he must pursue new or unusual avenues of inquiry. The history and physical examination assume renewed importance. The results of hematologic examinations, of histologic, cytologic, bacteriologic, and chemical analyses of stools, of specific serologic and immunologic tests, and finally of more or less specific therapeutic tests all are advanced in evidence and critically evaluated.

Although the histories of patients afflicted with these types of ulcerative colitis have, in general, marked degrees of similarity, significant points may often be elicited on the sole basis of which it may be possible to predict the ultimate diagnosis rather accurately. A history of rectal bleeding that has continued for weeks or months but has gradually increased in amount, that has been accompanied by diarrhea which developed insidiously but gradually increased in severity often to the point of being intractable, with remissions and exacerbations of both symptoms, points strongly to the existence of ulcerative colitis type I (thrombo-ulcerative). When dysentery develops in a case of pulmonary tuberculosis, if ulcerative colitis of any kind is present it will probably be tuberculous in origin (type 4). The history of a patient with dysentery will often show that he has been in a region where amebic dysentery has been endemic, and this gives an immediate clue as to the possible nature of the difficulty (type 5). The history of a patient with dysentery may also show that he has long subsisted on a diet ob-Lusly inadequate; in instances of this kind the clinician will conduct investigations along dietary lines (type 6). In ulcerative colitis type 2 and type 3 the history is just as lacking in distinguishing diagnostic features as are the pathologic

manifestations. The onset is usually severe, but may be mild; even though the stools and rectal discharges are not great in number, great depletion may take place rapidly. Disturbances of the upper part of the digestive tract are observed more frequently in this type of ulcerative colitis than in others.

In this series of patients with ulcerative colitis 62 (12.5 per cent) were less than twenty years of age; 305 (61 per cent) were between twenty and forty years of age; 115 (23 per cent) were between forty and sixty years of age; and only 18 (3.5 per cent) were more than sixty years of age. The youngest patient was an infant of fifteen months; the oldest was a man aged seventy-three years. Two hundred and seventy-nine patients (56 per cent) were males.

The cases were analyzed by type with respect to duration, degree of severity, and degree of anemia as indicated by determinations of the amount of hemoglobin in the blood. Patients with ulcerative colitis type I (thrombo-ulcerative) in general had symptoms for long periods of time, while patients with ulcerative colitis types 2, 3 and 4 (tuberculous) were ill for relatively short periods of time. In general, the symptoms of all types of ulcerative colitis were of moderate degrees of severity. Severest anemia was observed in cases of ulcerative colitis type I (thrombo-ulcerative). This is not a surprising finding since patients with this disease were ill longer and had occasion to suffer greater losses of blood than patients with the other types of ulcerative colitis.

As was pointed out earlier in this paper, the final or ultimate diagnosis in cases of ulcerative colitis is not always made on the occasion of the patient's first consultation with the physician. The diagnosis may be made with relative ease when all findings dovetail into what has become recognized as the typical clinical and pathologic syndrome of one of the better-known types of ulcerative colitis. This is usually the case. Experience with some of

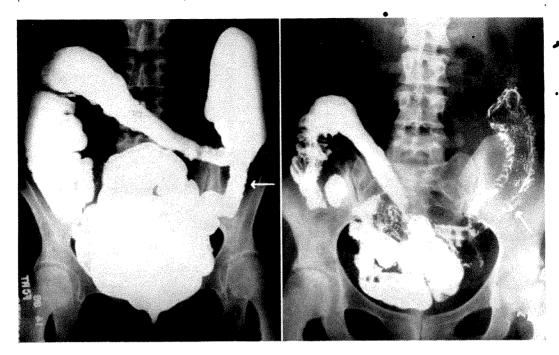


Fig. 1. Ulcerative colitis type 2; involvement confined to transverse colon, including both limbs of hepatic flexure, and to a short segment of descending colon (arrows); results of proctosigmoidoscopic examination negative.

the more rarely encountered forms of ulcerative colitis is so meager that we feel competent to draw but tentative conclusions about them. Sometimes, in all of the forms of ulcerative colitis, the patient is seen at a time when the pathologic process is so destructive that significant and pathognomonic features are effaced. In such instances it may be necessary to delay making the ultimate diagnosis until general and more or less specific therapeutic measures have succeeded in alleviating the acute and fulminating character of the process.

This study has emphasized again that neither the history and physical examination nor any single objective test is sufficient in all instances to provide the final diagnostic word in cases of ulcerative colitis. The final diagnosis is made and proper therapeutic measures are instituted only after all relevant diagnostic data are collected, carefully evaluated and properly correlated.

#### ROENTGENOLOGIC CONSIDERATION

Since the roentgenologic manifestations of all forms of chronic ulcerative colitis

reflect the gross morphologic changes which the pathologic process produces in the size, shape and contour of the part of intestine affected, the roentgenologic diagnosis is expected to be no more determinative than is the diagnosis made after gross pathologic examination. Anatomically, chronic ulcerative colitis of all types produces some degree of narrowing and shortening of the intestine, destructive or productive changes in the intestinal wall and ulceration on the mucosal surface. The intensity of the changes produced varies with such factors as the duration and extent of the disease, its virulence, and the amount of secondary infection. As was pointed out earlier in this paper, certain macroscopic features of the ulcerative process are so distinctive that the etiologic nature of certain forms of ulcerative colitis is often determined accurately by inspection of the mucosal surface of the intestine at proctosigmoidoscopic examination. Many of the particular features used in making the proctologic diagnosis are, however, not elicitable at roentgenologic examination because they are com-

posed of such visual elements as color, the nature and distribution of exudates, and very small differences in size and shape of small mucosal defects. On the other hand, the less delicate macroscopic changes, that is, the gross deformities, are not essentially pathognomonic because the processes by which they have been developed are essentially the same, whatever the cause of the disease. Roentgenologically demonstrable changes in the intestine produced by the ulcerative process are general contraction, which implies narrowing and shortening, productive and destructive changes in the intestinal wall, changes in mobility and flexibility as revealed by roentgenoscopically controlled manipulation, and destruction of the internal surface of the intestine as revealed by changes in the pattern of the mucosal relief. For diagnostic criteria, to be used in distinguishing the forms of ulcerative colitis from each other, the roentgenologic examiner is limited to such roentgenologically recognizable features as the site of earliest and severest involvement, the distribution of the process in the intestine, its methods and direction of extension, the general intensity of the disease, and the roentgenologic findings in other organs which might give a clue to the nature of the intestinal disease. In addition, the experienced observer may discern a peculiar roentgenologic "look" which enables him, intuitively almost, to postulate a diagnosis without being able to offer, to a less experienced roentgenologic observer, very acceptable reasons for doing so.

The roentgenologic manifestations of chronic ulcerative colitis type I (thromboulcerative), type 4 (tuberculous), and type 5 (amebic), have been described elsewhere. It is important to emphasize only that, while these have the most consistent roentgenologic syndromes of all forms of ulcerative colitis, in all instances the roentgenologic evidence must be carefully weighed and evaluated, preferably, of course, and sometimes of necessity, in collaboration with the clinician and proctoscopist.

The roentgenologic manifestations of the types of ulcerative colitis which we designated as types 2 and 3 deserve some comment. Review of the roentgenologic findings in these types leaves the impression that no single description could be made

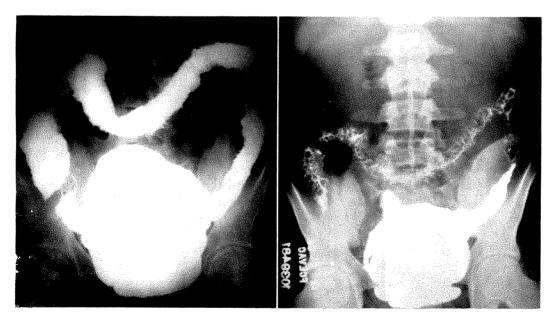


Fig. 2. Ulcerative colitis type 2; diffuse ulcerative colitis involving the entire colon above and including the descending portion; results of proctoscopic examination negative except for a single small rectal polyp; left, roentgenogram of colon distended with opaque enema; right, after evacuation of opaque enema.



to include all the manifestations in all of the cases. It is possible to divide them into two groups: one in which hyperplastic or productive elements predominate in the roentgenologic picture, and another in which ulcerative or destructive elements predominate. Thus the resemblance to intestinal tuberculosis is obvious; in fact when the ileum and cecum are both involved, a purely roentgenologic distinction denied. Most frequently, however, the roentgenologic appearance of the segments involved with this atypical form of ulcerative colitis has a destructive "look" (Figs. 2 and 3), and with experience a characteristic, irregular development of the process is readily recognized.

The roentgenologic appearance of the colon in the deficiency states (type () may superficially resemble that of one of the



Fig. 3. Type 3 ulcerative proctosigmoiditis at proctoscopic and roentgenologic examination; *left*, roentgenogram of colon distended with opaque enema; *right*, after evacuation of opaque enema.

between tuberculous and non-tuberculous ulcerative colitis cannot be made. If evidence of active pulmonary tuberculosis is elicited, the presumptive diagnosis is evident immediately. The irregular distribution of the lesions in types 2 and 3 is shown in Table II. The roentgenologic appearance may resemble that of type I very closely in every respect except the distribution (Fig. 1). That when this occurs, the disease may indeed be of the same etiologic nature as in type I cannot be

other types of chronic ulcerative colitis, but the resemblance is not, as a rule, marked. Because ulcers, when they have developed, are superficial, and because submucosal infiltration does not take place to a great extent, contraction either in length or in caliber is not observed. The caliber of the intestine tends, as a matter of fact, to be larger than normal. Marked atonicity of the bowel is one of the striking features. Combining with this are a marked reduction in the mucosal relief, an excessive

Live or

quantity of abnormal intestinal secretion which is probably responsible for the peculiar distribution of the contrast substance on the mucosal surfaces, and a striking inability of the intestine to contract and expel its contents efficiently. If this form of intestinal change is confused with other forms of ulcerative colitis roentgenologically, it is because the examiner, unfamiliar

ments were uniformly shortened and narrowed and there were definite changes in the mucosal relief, consisting in a complete absence of relief in the 2 cases in which the disease was designated as ulcerative colitis type I (thrombo-ulcerative) at roentgenologic examination (Fig. 4), and a deeply pitted relief pattern in the case in which the disease was classified roentgenologic.



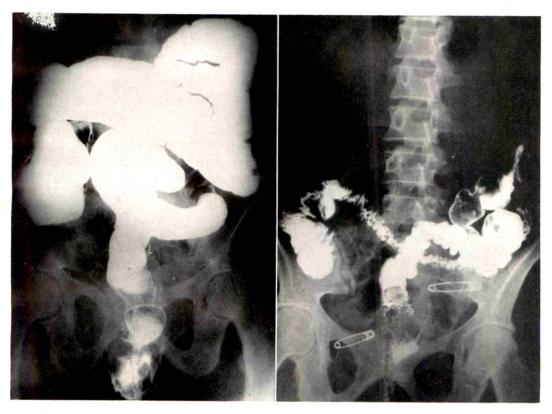


Fig. 4. Ulcerative proctosigmoiditis of lymphogranuloma venereum; Frei test positive; the patient was a legress, thirty-four years old; she also had a rectovaginal fistula which confuses the roentgenologic picture to some extent; the proctoscopic diagnosis was lymphogranuloma venereum; *left*, roentgenogram of colon distended with opaque enema; *right*, after evacuation of opaque enema.

with the clinical picture, finds himself at a loss to explain his findings on a basis other than an atypical ulcerative colitis. Frequently, in fact, the large intestine is entirely normal in the states of dietary deficiency.

In all the 3 cases of lymphogranuloma renereum (type 7) in this series there were significant roentgenologic findings. The involvement was confined to the rectum and lower part of the sigmoid. These segcally as type 3 (Fig. 5). Review of these and other cases in our larger series in which lymphopathia venereum has extended from its original site to involve the rectum and lower part of the sigmoid grossly indicates that a fairly typical roentgenologic syndrome might be developed by which at least a presumptive diagnosis of this disease might be rendered by using roentgenologic data alone.<sup>5</sup>

It is apparent, we believe, that no group

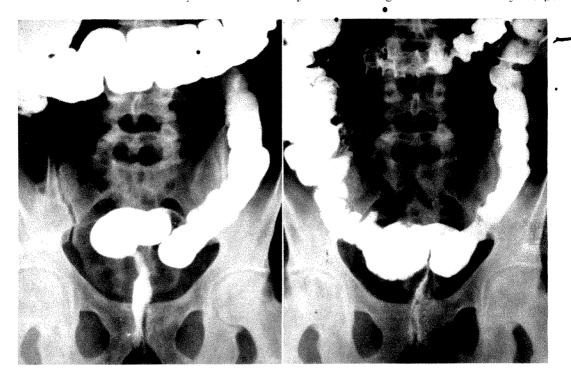


Fig. 5. Lymphogranuloma venereum affecting a white man, thirty-five years old; Frei test positive; proctoscopic diagnosis was lymphogranuloma venereum; *left*, roentgenogram of colon distended with opaque enema; *right*, after evacuation of opaque enema.

of patients requires a more intelligent and complete mobilization of all diagnostic facilities than those with one of the types of ulcerative colitis. No single group of human maladies lends itself better to careful objective analysis than this. The stools are readily examined both with the naked eye and microscopically. The lesions of the rectum and sigmoid are observed directly with the proctosigmoidoscope. The changes produced by the disease above the level of proctosigmoidoscope reach come under observation with roentgenologic methods. Progress in the way of diagnostic refinements continues to be made, and we feel that it is logical to expect that therapeutic advances will not lag far behind.\*

#### REFERENCES

- 1. Bargen, J. A., and Weber, H. M. Regional migratory chronic ulcerative colitis. Surg., Gynec. & Obst., 1930, 50, 964-972.
- 2. Bargen, J. A., Jackman, R. J., and Kerr, J. G. Studies on the life histories of patients with chronic ulcerative colitis (thrombo-ulcerative colitis), with some suggestions for treatment. *Ann. Int. Med.*, 1938, 12, 339–352.
- 3. Buie, L. A. Practical Proctology. W. B. Saunders Company, Philadelphia, 1938, 512 pp.
- 4. Buie, L. A., and Bargen, J. A. Chronic ulcerative colitis; a disease of systemic origin. J. Am. M. Ass., 1933, 101, 1462–1466.
- 5. WEBER, H. M. Unpublished data.
- 6. Weber, H. M. The roentgenologic identification of commonly encountered chronic ulcerative diseases of the colon. Am. J. Roentgenol. & Rad. Therapy, 1933, 30, 488-496.



<sup>\*</sup> For discussion see page 841.

# THE SURGICAL TREATMENT OF ULCERATING GASTRIC LESIONS

#### WITH CORRELATED ROENTGENOLOGIC STUDIES\*

By WALTMAN WALTERS, M.D. Division of Surgery, The Mayo Clinic ROCHESTER, MINNESOTA

T IS a great pleasure to have this opportunity to express my appreciation to the members of the American Roentgen Ray Society for their contributions to the diagnosis of surgical lesions of the stomach. Although a carefully taken history and a properly performed physical examination will indicate, in many cases, the nature of the lesion producing the patient's symptoms, confirmatory evidence furnished by roentgenoscopic and roentgenographic examinations not only serves as a visual method of confirming the diagnosis and exact situation of the lesion but in many instances affords an excellent idea not only of its extent, but frequently, the pathologic nature of the lesion. This method of examination, therefore, affords the greatest aid in localizing lesions of the stomach or in eliminating the stomach as the cause of the patient's dyspepsia. It is surprising in some cases, however, how late in the course of the patient's treatment roentgenologic examinations have been made. Treatment is sometimes carried out entirely on the basis of a diagnosis made on a clinical history of dyspepsia not unlike that associated with benign ulceration. On innumerable occasions one encounters patients having carcinoma of the stomach, many of them in advanced stages of the disease, who have been under medical dietary treatment for months, and sometimes years, on the erroneous assumption that benign ulceration of the stomach or duodenum was present. This is largely a result of the fact that the history and early stages of the disease were particularly like those of benign ulceration and prompt symptomatic response was obtained by

resorting to frequent feedings and alkalies. Only later, when relief was not obtained by such means, was the roentgenologic examination made showing the malignant nature of the lesion.

In discussing carcinoma of the stomach I have repeatedly emphasized this point, following it with the corollary that no patient should be placed on a medical regimen for what seems to be a benign lesion of the stomach or duodenum without its being first ascertained by roentgenologic examination whether the lesion is in the stomach or duodenum. If it is in the stomach, the possibility that the lesion may be malignant in spite of the fact that it does not appear so on the initial roentgenologic examination should always be kept in mind. This also holds in cases in which the lesion may seem to disappear, roentgenologically, under a medical regimen. Such patients should not be lost sight of until repeated roentgenologic examinations have revealed complete disappearance of the lesion and until the patient's symptoms have been completely relieved. The fact that more than 95 per cent1 of gastric lesions can be demonstrated by the roentgenologist is a real achievement. The internist and surgeon must nevertheless remember that, with approximately a 5 per cent error in roentgenologic examinations of the stomach, the patient who appears by the clinical history to have a gastric lesion but for whom results of a roentgenologic examination were negative should not be dismissed without the admonition that other roentgenologic examinations be made at intervals of two or three months. Better still,

<sup>\*</sup> Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, III., Sept. 19-22, 1939.

if a competent gastroscopist is present, as should be the case, gastroscopic examination should be combined with repeated roentgenologic examinations in an attempt to ascertain for certain that no intragastric lesion is present.

# MALIGNANT GASTRIC LESIONS SIMULATING BENIGN ONES

When roentgenologic examinations demonstrate seeming localization of the lesion in the duodenum, it would seem to be rather conclusive evidence that the lesion is benign, for the first part of the duodenum is one of the rarest sites for primary malignant lesions to develop. However, there is a group of patients in whom ulcerating lesions of the lesser curvature of the stomach, because of associated gastric spasm and interference with gastroduodenal motility, produce roentgenologic data which may be misinterpreted as pyloric or duodenal obstruction. This may lead to the erroneous localization of the lesion in the duodenum when in reality it is in the stomach. The following 3 cases are illustrative.

#### REPORT OF CASES

CASE 1. A woman, aged forty-three, came to The Mayo Clinic on January 6, 1938. For twenty-two years she had had ulcer-like distress and had been following a diet for ulcers since August, 1937. The gallbladder had been removed in 1928 and she had had some relief for a short time following this operation. She complained of fullness after meals and occasionally had experienced pain at night. She had vomited old food on an average of once a week and recently, three times a week. Alkalies and milk gave relief. A roentgenologic diagnosis of duodenal ulcer with obstruction and considerable secondary dilatation of the stomach was made. The patient underwent operation on January 10, 1938, partial gastrectomy with Billroth I anastomosis being performed. The lesion was reported by the pathologist to be a Grade 1 colloid adenocarcinoma, situated at the pyloric end of the stomach. No duodenal ulcer could be distinguished. After an uneventful convalescence, the patient was dismissed on January 28, 1938. In a letter dated December 14, 1938, she wrote

that she was feeling and sleeping better than in many years, that her appetite was fairly good—and that she was able to eat almost all kinds of food

CASE II. A man, aged fifty, registered at The. Clinic on October 6, 1938. He had had epigastric distress after meals for two years, with relief from food never more than 75 per cent of the time. He had had no nausea, vomiting, hematemesis or melena. He had lost 23 pounds (10 kg.) in the past two years. He had been following a diet for ulcers without much relief. Roentgenologic examination of the stomach disclosed a duodenal ulcer with a crater. Gastric analysis revealed anacidity and because of observation it seemed advisable to perform astroscopy; this was done on October 11, 1938. However, no lesion could be seen in the stomach to account for the patient's symptoms, although a satisfactory view of the upper portion of the stomach could not be secured because of excessive secretion At operation on October 14, 1938, multiple carcinomas of the stomach were found, and total gastrectomy was performed. There was also marked hemorrhagic gastritis and chronic duodenitis. The patient died on October 19, 1938, of bronchopneumonia.

CASE III. A man, aged fifty-nine, returned to The Clinic on December 6, 1938. In 1909 drainage of his gallbladder had been performed and the opening to his stomach had been dilated. In 1914 partial cholecystectomy and appendectomy had been performed, and on March 15, 1924, cholecystectomy had been performed. Examination of the duodenum at the time of cholecystectomy disclosed a condition that was suspiciously like an ulcer on the anterior wall, but a positive diagnosis of duodenal ulcer could not be made because of the amount of adhesions remaining from the previous operation. For three years before returning to The Clinic in 1938, the patient had had intermittent attacks of epigastric pain two or three hours after meals; this distress was relieved by food and soda. He also had experienced frequent pain at night, with extension to the back. He had occasionally vomited during the spring of 1938 and also about three months have fore coming to The Clinic. He stated that his stomach felt full after meals and it seemed to require a long time for it to empty. The roentgenologic examination showed a duodenal ulcer and deformity of the stomach situated under the scar of the gallbladder. At operation on December 16, 1938, carcinoma on a gastric ulcer was found, and partial gastrectomy, with posterior Polya anastomosis and partial duodenectomy, was performed. Chronic gastritis and chronic duodenitis were also present. The patient's convalescence was uneventful and he was dismissed on January 9, 1939.

These 3 cases were the only ones of this type which came to my attention during 1938. I mention this because, although the possibility of error exists, fortunately the condition occurs infrequently. It is a point, however, which I think should be emphasized, especially to the internist who favers the nonsurgical treatment of all duodenal ulcers unless they constitute surgical emergencies.

# DIFFERENTIAL DIAGNOSIS OF BENIGN AND MALIGNANT GASTRIC ULCERATION

In the Annual Oration for 1936, delivered before the Medical Society of London, Sir James Walton said, when referring to carcinoma of the stomach secondary to peptic ulceration: "Today the figures of Stewart are generally accepted. ... Nine and one-half per cent of cases of chronic ulcer become carcinomatous and 17 per cent of cases of carcinoma originate in a chronic ulcer." Quoting further, Walton said: "Clinical criteria are notoriously unreliable . . . . The history of carcinoma in its early stages may also closely resemble that of chronic ulcer, so that an even higher percentage of the cases diagnosed clinically as chronic ulceration become malignant . . . . In early cases the diagnosis of carcinoma may only be possible on microscopic examination, while in the later stages the mass of growth may be so extensive that it is impossible to determine with the naked eye whether the ulcer is primary or secondary. Microscopic examination will nevertheless often reveal characters of the original ulcer."

It seems to me that Walton has concisely stated the case against gastric ulcer from the standpoint of the menace of carcinoma. When to this statement is added

Katsch's figure that a gastric ulcer has a 20 per cent chance of being malignant, it emphasizes the necessity of attempting to differentiate between the benign gastric ulcer and the gestric ulcer with malignant changes. I wish to call your attention particularly to this point because it is by the earlier recognition of malignant changes in such small lesions that we are going to be able not only to increase the number of people having carcinoma of the stomach who can be operated upon, but also, an excellent opportunity will be afforded of prolonging the patient's life and obtaining a cure in such cases by partial gastrectomy. Unfortunately, the wave of enthusiasm which a few years ago was evident in certain parts of the country to advise medical treatment in all cases in which a roentgenologic diagnosis of gastric ulcer was made led to the postponement of necessary operations. In these cases, particularly in those in which the ulcer was large and perforating in character, not only was relief of symptoms temporary but little change was noted in the size of the lesion. In addition, with the passage of time it was found that a few of the lesions had been carcinomatous ulcers and not benign ones. Unfortunately, in some of these cases the delay plus the rapidity of growth of the lesion made surgical removal difficult and in some cases, impossible. Although in the last two or three years the viewpoint regarding the management of such lesions has improved, there are still those physic ans who have failed to be impressed by the fact that whereas the report of a malignant gastric ulcer by the competent roentgenologist is usually a correct one, Kirklin has pointed out that the roentgenologic report that a lesion is a gastric ulcer does not exclude its being carcinomatous. On many occasions wherein lesions have been reported preoperatively as being malignant because the meniscus sign-complex of Carman and Kirklin was present, I have thought at operation on the gross appearance of the lesion that it might be benign, only to have the patholo-



Fig. 1. Large, recurring, perforating gastric ulcer situated high on the lesser curvature of the stomach. (Published by permission of the *American Journal of Surgery*.)

gist report it as being malignant on microscopic examination. At The Clinic we assume that every ulcerating lesion of the stomach is malignant until it is proved to be benign.

The medical critics of the surgical treatment of ulcer, in supporting their thesis that medical treatment of all gastric ulcers should be carried out, like to substantiate their argument by saying that less than 10 per cent of the ulcers are malignant or become malignant and that, in view of this fact and the high risk entailed in the removal of the ulcer, medical treatment always should be undertaken. These arguments, it seems to me, are fallacious when it is known that more than 10 per cent of such lesions actually are malignant and when it is considered that the risk of removing either a gastric or duodenal ulcer in the hands of surgeons experienced in gastric surgery is exceedingly low. In point of fact, sixty-two operations were performed for nonperforated gastric ulcer at The Mayo Clinic in 1938, with a mortality rate of 3.2 per cent. Three hundred and forty-three operations were performed for nonperforated duodenal ulcer during the same period, with a mortality rate of 1.2 per cent. Partial gastrectomy was performed for benign lesions of the stomach and duodenum in 215 cases, with a mortality of 2.8 per cent.

There is another lesion, the early recognition of which is important been be frequently it contains malignant recognition periphery, and this lesion is the property of the fact that many of these polyps do contain malignant cells in the eriphery of the lesion and the fact that the roentgenologist is able to demonstrate the presence of these lesions in most instead when they are no larger than one's mail, should lead to their earlier recognition and removal, particularly in those cases in which secondary anemia is present, for many of these polyps produce silent bleeding.

It is a routine at The Clinic to examine the stomach and colon of all patients who have marked anemia, even though the morphologic picture of the blood would seem to indicate that the anemia was of the primary type. It has been a surprise to many of us how frequently bleeding polyps have been demonstrable in these regions in such cases, many of which lesions have been removed surgically, resulting in disappearance of the anemia.

#### THE OPERABILITY OF GASTRIC LESIONS

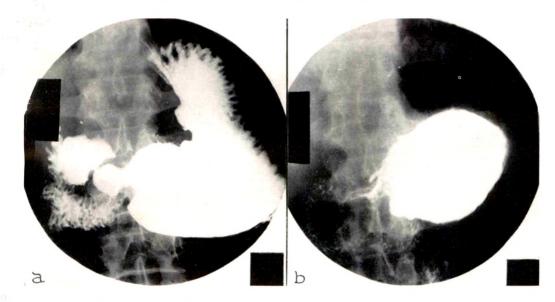
Gastric ulcers situated high on the lesse. curvature and those situated high on the posterior wall of the stomach are quently reported, on the basis of roentgenologic examination, to be of questionable accessibility to surgical removal. Their high situation is likely to be considered an additional reason for continuation of medical treatment which has failed to cause healing of the ulcer previously. That all benign gastric lesions are accessible to surgical treatment is, therefore, a point which deserves emphasis. On several occasions, because of the perforating nature of the lesion and its attachment, particularly to the capsule of the pancreas, and because of contraction and fixation of

the stomach in the vicinity of the lesion, the appearance has been that the lesion was higher than it really was.

In a case in which I operated two years ago, a man of sixty-eight years had a large, recursing, perforating gastric ulcer, 3 cm. in the lesser curvature (his in No evidence of healing of the unit curred on medical treatment. The reason the ulcer seemed so high was that it had the forated and attached itself to the

In addition to these methods, the transgastric method of removal of some of the ulcers on the posterior wall, at the fundic end of the stomach, has given very good results.

In reviewing the problem of carcinoma of the stomach, Cranston Holman stated: "Up to the present time surgery offers the only satisfactory means of treatment and, as the methods of Billroth and their various modifications are still considered techni-



3. 2. a, perforating gastric ulcer (hemorrhagic) on the lesser curvature; b, postoperative roentgenogram following Billroth I resection of the stomach and the gastric ulcer. (Published by permission of the American Journal of Surgery.)

capsule of the pancreas and to the gastrocolic omentum. When the ulcer was freed from its attachment to the pancreas, it was found that there was a considerable amount of normal stomach above it, which enabled performance of satisfactory partial gastrectomy of the Polya-Balfour type.

Removal of that portion of the lesser curvature which contains a gastric ulcer, as in the Billroth 1 or the Hofmeister-Polya resection, enables the surgeon to preserve a sufficient amount of the body of the stomach, and particularly the greater curvature, for its anastomosis with the duodenum or with the jejunum (Fig. 2a and b).

cally adequate, it is doubtful whether in the future any startling advances will be made in the technical approach to curing carcinoma of the stomach." While in general I agree with this opinion, it would appear that, with increasing experience in gastric resection, particularly that for malignant disease of the stomach, the greater the experience of the operator in this field the greater will be the number of cases in which gastric resection will be performed. In some of the American clinics there has been a progressive increase in the percentage of cases in which gastric resections have been performed; or, in other words, greater operability has been attained in some clinics by willingness to resect from three-fourths to four-fifths of the stomach without hesitancy when the lesion is confined to the stomach and, in a few cases, even to perform total gastrectomy. Last year at The Mayo Clinic in 251 cases in which operations were performed for malignant neoplasms of the stomach, partial gastrectomy was performed in 124 cases, or an operability rate of 49.4 per cent, with a mortality rate of 13.9 per cent.

In 1937,8 at the Inter-State Post-•Graduate Medical Assembly of North America, in discussing carcinoma of the stomach, I called attention to the fact that the advances made in the previous year in the treatment of carcinoma of the stomach might be attributed in part to: (1) increased operability as result of accepting for exploration all patients having carcinoma of the stomach, provided their general condition does not contraindicate it and provided metastasis cannot be demonstrated (in 1938 at The Mayo Clinic operation was performed for 61.4 per cent of all patients having carcinoma of the stomach), and (2) willingness to perform as extensive a resection as necessary, even to the extent of subtotal or total gastrectomy in order to remove a malignant lesion confined to the stomach or its adjacent glands. [Resections of the stomach were performed on 48.8 per cent of patients having carcinoma of the stomach operated on in 1938; in 1937 the rate for resection was 49.3 per cent and in 1936 it was 45.3 per cent.]

It is apparent, therefore, that not only is a larger group of patients having carcinoma of the stomach being explored but within this larger group a larger number is having partial gastrectomy performed.<sup>7</sup>

On many occasions I have seen malignant lesions of the stomach, which, on roentgenologic examination seem to encroach on the upper third of the stomach, but at operation there was found to be considerably more uninvolved stomach above the lesion than appeared to be the case in the roentgenologic examination. So frequently has this been the case and so

extensive have been the resections for malignant lesions of the stomach at The Clinic in the past few years that it seems to me that our roentgenologists have modified their viewpoint regarding operability by indicating as inoperable only those cases in which most of the cardiac end of the stomach is involved. Although this procedure sometimes makes it difficult for the surgeon to explain why he is unable to remove a lesion which the rentgenologist reported as being operable, it accomplishes a far more important purpose in permitting surgical exploration for a larger group of patients, some of whom will be found to have operable lesions.

The corollary of this substantiates the argument that all patients having malignant lesions of the stomach, no matter how extensive, should be given the benefit of abdominal surgical exploration, provided distant metastasis cannot be demonstrated.

It has been our experience at The Clinic that in from 15 to 18 per cent of patients in whom a malignant gastric lesion has been reported to be of doubtful operability or inoperable it was found, on exploration, that the lesion could be, and was, therefore, removed.

A few years ago my assistant, Dr. Norman Thiessen, several of my celleagues, and I<sup>6,7</sup> were interested in carrying out a follow-up study of cases of this type in which three-fifths or more of the stomach had been removed at operation. We found 184 consecutive cases between the years of 1918 and 1931. It was with the greatest satisfaction that we noted that 33 (17.93 per cent) of these patients were living and well without evidence of recurrence five years or more following partial gastrectomy. The preoperative roentgenologic diagnosis in 129 of the 184 cases was "operable," in 40 cases, "operability doubtful," and in 15, "inoperable." Of the 15 patients for whom the preoperative roentgenologic report had been "inoperable" and upon whom partial gastrectomy was performed, I patient lived twelve years, I lived eight years, and 2 patients lived six

years. Sixteen patients who lived five or more years after operation had had involved lymph nodes at the time of operation. These patients, then, could be considered to be "pure salvage."

#### SUMMARY AND CONCLUSIONS

Roentgenologic examination of the stomach affords a great aid in recognizing and localizing lesions of the stomach or eliminating the stomach as the cause of the patient's dyspepsia. The supplementary value of the gastroscopic examination as a check on the roentgenologic report, particularly in patients with a clinical history of a gastric lesion but the results of whose roentgenologic examinations have been negative, will serve to decrease the error in the diagnosis of intragastric lesions by these two methods to a minimum.

Since many patients who have carcinoma of the stomach in the early stages have a history suggesting peptic ulcer, it should not be assumed that such patients have benign lesions of the stomach or duodenum until the same is proved by roentgenologic examination and until the presence of an intragastric malignant lesion is excluded. In an occasional case, a malignant gastric ulcer will produce sufficient pylorospasm to lead to the erroneous assumption that the lesion is in the duodenum and is benign, when in reality it is in the stomach and may be malignant. The possibility of this error should always be borne in mind and whenever the guestion arises, gastroscopic examination would be of great assistance in localizing the lesion in, or excluding it from, the stomach.

Experience has shown that the report by the roentgenologist that a gastric ulcer is malignant is practically always correct, but the report that a gastric ulcer is present and that it is benign does not exclude its being malignant. Accumulating evidence would seem to indicate that the percentage of gastric ulcers that \*are malignant as well as the number of malignant lesions which start as gastric ulcers is much nearer 20 per cent than 10 per cent.

In the case of patients who have anemia, roentgenologic examinations of the stomach and colon have frequently shown that a bleeding polyp is the cause of the anemia. Many of these polyps contain malignant cells in their periphery and their early recognition and removal may prevent the development of an extensive malignant lesion. It is a great triumph for the roentgenologists that they can demonstrate polypoid lesions of this type that are as small as 0.5 cm. in diameter.\*

#### REFERENCES

- I. GRAY, H. K., BALFOUR, D. C., and KIRKLIN, B. R. Cancer of the stomach. Am. J. Cancer, 1934, 22, 249-286.
- 2. Holman, Cranston. The diagnosis of gastric carcinoma and peptic ulcer; the comparative value of various procedures, with special reference to the gastric analysis. J. Am. M. Ass., 1937, 108, 1383–1385.
- 3. Katsch. Quoted by Hurst, A. F. Carcinoma of the stomach. *Lancet*, 1937, 2, 1455.
- 4. Kirklin, B. R. Roentgenologic distinction of benign from malignant ulcerating lesions of the stomach. J. Michigan M. Soc., 1937, 36, 453-457.
- 5. Stewart. Quoted by Walton, ref. 10.
- THIESSEN, N. W. Results of subtotal gastrectomy. Proc. Staff Meet., Mayo Clin., 1935, 10, 582-584.
- 7. Walters, Waltman. The treatment of extensive malignant lesions of the stomach. J. Am. M. Ass., 1934, 103, 1345–1348.
- 8. Walters, Waltman. Carcinoma of the stomach. *Proc. Inter-State Post-Grad. M. A. North America*, 1937, pp. 86-91.
- Walters, Waltman, Binger, M. W., and Eusterman, G. B. Gastric lesions of doubtful operability. Proc. Staff Meet., Mayo Clin., 1935, 10, 584-588.
- 10. Walton, James. Carcinoma of the stomach. Lancet, 1936, 1, 1101-1107.
  - \* For discussion see page 841.



# THE DIFFERENTIAL DIAGNOSIS OF PYLORIC AND PREPYLORIC ULCERATION\*

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THE demonstration of ulcerative lesions in the pyloric and prepyloric areas has become increasingly easy due to the improvement of roentgenologic technique but it cannot be truly said that their differential diagnosis has improved in like manner. This area is particularly important because in it occurs a majority of all gastric carcinomas, benign gastric tumors, and cases of gastric syphilis. It is also a favorite location for the occurrence of benign gastric ulcer, spastic phenomena, and hypertrophic pyloric stenosis.

It is now universally accepted that the differentiation between benign and malignant ulceration in this area cannot always be accurately made by means of the roentgen examination alone. We need the help of every clinical aid which is available, and the final diagnosis must of necessity rest upon careful study of serial sections of the resected lesion. It is well known that carcinoma of the pyloric area may simulate benign lesions clinically and may show a considerable amount of relief following the use of medical ulcer therapy. This relief may persist for some months during which time the malignant process continues to progress.

In this study we are limiting ourselves to lesions of the pyloric ring and the prepyloric area within I inch of the pylorus. All of the cases to be reported are those in which the lesions have been resected and careful pathological studies made of the ulcerated areas.

While we do not intend to enter into a detailed review of the literature on this subject, it is necessary to refer briefly to several articles in order to more fully outline the subject we wish to discuss. Camp¹ states that in the region of the pylorus we

are concerned chiefly with the differential diagnosis of malignant neoplasms benign ulcer, pylorospasm, syphilis, and hypertrophic pyloric stenosis. He also states that in the pyloric area carcinoma greatly outnumbers benign ulcer, and that prepyloric ulcer has a greater predilection for undergoing malignant degeneration than ulcers elsewhere in the stomach. Holmes and Hampton,<sup>3</sup> in a study of the material from the Massachusetts General Hospital, found that the relative proportion of benign to malignant prepyloric ulcerations was approximately 1 to 12. They believe that any chronic, indurated lesion occurring in the pyloric antrum within I inch of the pylorus but not involving it should be considered malignant until proved to be benign. They believe it wise to surgically remove all such lesions rather than to use medical or palliative treatment. Singleton<sup>6</sup> studied the cases of prepyloric ulcer from the Toronto General Hospital. In 7 cases, where the lesion occurred within I inch of the pylorus, partial gastrectomy was done and microscopically the lesions in all cases were found to be benign gastric ulcer. He also reported 4 cases of malignant ulcer in the prepyloric segment. In 3 of these the roentgen picture was that of malignant neoplasm. Jensen and Rivers<sup>4</sup> state that it is extremely difficult, in lesions of the pyloric ring, to arrive at an accurate diagnosis even though all means at the disposal of the clinician are utilized. They estimate that in about 15 per cent of cases with pyloric lesions they are unable to be certain that the lesions are not malignant. They therefore recommend surgical exploration for patients who are found to have such deformities.

In the series of cases we are reporting are

<sup>\*</sup> Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19-22, 1939.

but do not state the percentage of cases actually found to be malignant. Holmes and Hampton<sup>3</sup> found the relative proportion of benign malignant ulceration in the prepyloric area to be approximately I to 12. Singleton<sup>6</sup> reported 7 cases of benign prepyloric ulceration and 4 cases of malignant neoplasm of the same area. It should be noted, however, that 3 of the latter cases were diagnosed as being malignant preoperatively, which type does not belong in the category under consideration here.

In this series of 35 cases there were 24 cases of benign ulceration and 7 cases of malignant neoplasm, or 69 per cent and 20 per cent respectively. In the benign ulcer group 8 were located in the pyloric ring and 16 were located in the prepyloric area. In the malignant group 2 were located in the pyloric area and 5 in the prepyloric area. In addition there were 3 cases of chronic gastritis and 1 case of gastric syphilis.

There are some who object to resection because of the operative mortality but in this series there was only I postoperative death, or approximately 3 per cent. This death occurred from pulmonary gangrene one month postoperatively. This operative mortality is far less than the mortality which would have occurred in the cases of carcinoma in this group if they had not been resected early.

#### SUMMARY

A differential diagnosis between malignant neoplasm and benign ulcer cannot be made in all cases of pyloric and prepyloric ulceration by means of the roentgen examination.

An early diagnosis is very important in lesions occurring in this area, as they are easily resectable while in the localized stage and the percentage of cure is high.

In all such chronic indurated ulcerated lesions there will be a probable occurrence of malignant neoplasm in from 15 to 30 per cent of the cases.

If ulcers in these areas are treated medically they must be regularly checked at short intervals by roentgenologic examination, and resection advised if there is not prompt and sustained disappearance of the lesion.\*

#### REFERENCES

- CAMP. J. D. Roentgenologic significance of pyloric and prepyloric deformities. *Radiology*, 1931, 16, 847-855.
- Golden, R. Antral gastritis and spasm. J. Am. M. Ass., 1937, 109, 1497–1500.
- 3. Holmes, G. W., and Hampton, A. O. Incidence of carcinoma in certain chronic ulcerating lesions of the stomach. J. Am. M. Ass., 1932, 00, 005-009.
- 4. Jensen, R. M., and Rivers, A. B. Carcinoma or ulcer involving the pyloric ring: differential diagnosis. *Proceed. Staff Meet.*, *Mayo Clin.*, 1939, 14, 1-4.
- KIRKLIN, B. R. Roentgenologic distinction of benign from malignant ulcerating lesions of the stomach. J. Michigan M. Soc., 1937, 36, 453-457.
- 6. Singleton, A. C. Benign prepyloric ulcer. *Radiology*, 1936, 26, 198–208.



<sup>\*</sup> For discussion see page 841.

## SYPHILIS OF THE STOMACH

#### WITH A REPORT OF AN UNUSUAL CASE\*

By CLARENCE N. McPEAK, M.D. FITCHBURG, MASSACHUSETTS

SYPHILIS of the stomach is frequently described as being an extremely rare lesion, yet at least 115 authentic cases have been observed at the Mayo Clinic (Eusterman<sup>8</sup>). Any disease of which that many cases have been observed in one clinic cannot truly be termed as being extremely rare, but it is an uncommon finding.

The paucity of syphilitic involvement of the stomach found at autopsy is frequently stressed, but there are many factors which might account for this. It is hardly ever the cause of death, and unless one is specifically looking for it, the involvement of the stomach may be easily overlooked, as it is not as firm to palpation as is carcinoma.

The most important cause for the belief that syphilitic involvement of the stomach is extremely rare has been the insistence of many writers on pathologic confirmation before accepting the diagnosis. Just why this confirmation should be necessary is not clear when it is not considered necessary before accepting the diagnosis of syphilis of other organs. As there are no histopathologic findings that are pathognomonic of syphilis of the stomach, and as the pathologist rarely can make a positive diagnosis of the condition, it can readily be seen that to insist on this confirmation will exclude almost all of the cases reported in the literature. The microscopic examination is the least accurate of all of the methods of making the diagnosis. The gross pathology of the disease is much more typical than is the histopathology, and the surgeon should be familiar with the gross pathology in order to make the diagnosis at the operating table. Frozen sections taken at the time of operation are of no value in making the diagnosis except to exclude the presence of a neoplasm. Pusch<sup>26</sup> states that "in every case one searches in vain for a histopathologic lesion which is absolutely specific for syphilis." The value of the microscopic examination lies in excluding the presence of some specific pathology other than syphilis, and in this it is very valuable.

Some authors have demanded that the Treponema pallidum be demonstrated in the tissue. McNee<sup>17</sup> reported a case in which numerous spirochetes were demonstrated in a lesion in the stomach and he concluded that they were the Treponema pallidum. It is impossible to differentiate the Treponema pallidum from other spirochetes on microscopic examination of tissues. Singer and Dyas<sup>27</sup> assert that the dark field examination is the only means of accurately identifying the Treponema pallidum and that it is impossible to do so on stained slides. Spirochetes, indistinguishable from the Treponema pallidum, are frequently seen in sections taken from lungs in cases of fusospirochetosis and are also frequently found in ulcerated lesions in the stomach, usually within the zone of bacterial invasion but sometimes seen deeper. Rabbit inoculation of suspensions of macerated lesions is also inconclusive due to the fact that the spirochete of the naturally occurring rabbit spirochetosis cannot be distinguished from the Treponema pallidum (Noguchi<sup>22</sup>). It must be remembered that any or all organisms normally, or incidentally, present on the gastric mucosa, including the spirochetal saprophytes (for man) associated with any ulcerative lesion, would be present in the suspension of the macerated gastric lesion (Pusch<sup>26</sup>).

Syphilis of the stomach is most fre-

<sup>\*</sup> From the Department of Roentgenology of the Addison Gilbert Hospital, Gloucester, Massachusetts. Read at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.

quently mistaken for carcinoma, and many of the gastric resections performed on these cases have been done on the erroneous diagnosis of carcinoma.

. Most cases occur in the third or fourth decades of life, but several cases have been reported in the fifth and sixth decades, so that the age of the patient cannot definitely be used to exclude the presence of syphilis of the stomach. The case which I will report was sixty-two years of age at the time of the first observation seven years ago.

The symptomatology is proportionate to the extent of the pathology, obstruction and ulceration which exists in the stomach. Many patients give a history typical of gastric ulcer while others will have a history suggestive of carcinoma. There may be pain which may, or may not, be associated with eating and may, or may not, be relieved or aggravated by food. Vomiting is a frequent occurrence and may relieve the pain temporarily. Hemorrhage will occur in about 50 per cent of the cases. In advanced cases in which the volume of the stomach is markedly reduced, there will be difficulty in swallowing solid foods or complete inability to swallow them. The lower end of the esophagus may become dilated due to the diminished volume of the stomach. The patient will lose much weight but is not as ill looking as is the case with carcinoma. There is usually an absence of hydrochloric acid in the gastric secretions and histamine usually fails to stimulate its production. Eusterman7 and O'Leary23 found that 20 per cent of the cases at the Mayo Clinic had a palpable tumor, and a definite sense of resistance was noted over the involved area in most cases in which the patients were thin and dehydrated; 27 per cent had other manifestations of the disease; 73 per cent had a positive Wassermann reaction as the only other manifestation of the disease; and 6 per cent had a negative Wassermann reaction.

Gordon<sup>11</sup> reported a case in which he used thorium dioxide injection to rule out

the presence of metastases in the liver, as an aid in differentiation between syphilis and carcinoma of the stomach. This procedure I cannot advocate. Carcinoma of the stomach may be present without metastases in the liver so that a negative finding is of no value. The dangers of late sequelae following the use of thorium dioxide have frequently been stressed in the literature and I feel that these outweigh any advantage that may be gained by its

#### GASTROSCOPIC FINDINGS

The advent of the flexible gastroscope is so recent that it has not been used in a sufficient number of cases of syphilis of the stomach to give a complete picture of the findings. I believe that it will be of great value in the future as an aid in the differential diagnosis between syphilis and carcinoma of the stomach. This examination should be of particular value in cases in which ulcerations are present.

No specific findings have been observed in all cases. The mucosa may appear red flecked and rough with thick swollen folds and hypertrophic changes. Gutzeit and Teitge<sup>12</sup> state that cases of syphilis with primary lesions and with skin eruptions show nothing on gastroscopic examination or only a mild superficial catarrh. The treated and healed syphilitic patients showed superficial catarrh with atrophic changes, sometimes atrophic gastritis, rarely hypertrophic gastritis, more often a swollen condition of the mucosa. In latent syphilis a smooth condition of the mucosa was seen, regardless of whether the patient had, or had not, received treatment, and in tabes a similar condition, with hypertonicity (or contracture). Their conclusion was that the tendency in syphilis, where any change in gastric mucosa occurs, is toward the atrophic state.

Moutier<sup>21</sup> divides the cases into those showing tumor (gumma) formation and leaving a localized scar on healing; ulcerative forms, single or multiple, also on healing leaving scars with more contracture or distortion of the stomach (hourglass); and those showing a generalized gastritis, often hemorrhagic, resulting in atresia by submucosal involvement. Carey and Ylvisaker³ report a case with their observations during treatment and after interruption of these treatments.

#### PATHOLOGY

There are no pathognomonic findings in the microscopic or macroscopic examination of syphilis of the stomach. The gumma is the classical lesion of syphilis but rarely, if ever, is found in the stomach. Gummatoid areas may sometimes be found which will strongly suggest the nature of the pathology, but usually even these will be absent. The most common finding is a granulomatous thickening and induration of the wall of the stomach. The induration is pliable and is not hard, gritty, granular or friable as is the case in carcinoma. This pliability is due to the marked edematous character of the submucosa which is thickened out of all proportion to the thickening of the other layers of the stomach. In addition to the edema the usual features of a chronic inflammatory process are seen such as fibrous tissue proliferation, local and diffuse lymphocytic and plasma cell aggregations, with few polymorphonuclear cells, the infiltration being especially perivascular. These changes will be found throughout the wall of the stomach in the involved areas, but will be most marked in the submucosa. Occasionally gummatous areas with epithelioid cell and giant cell centers and lymphocytic and fibroblastic peripheries will be found. These lesions are not typical gummata and there are no criteria by which they may be definitely distinguished from tubercles. Much has been said concerning involvement of arterioles and venules leading to obliterative vasculitis, and it is claimed that these may play a part in the mechanism of necrosis and ulceration, but these features may be seen in any inflammatory process of long duration.

The histopathology depends upon the

area from which the section was taken. In cicatricial areas fibrous tissue changes will predominate; if taken from an area showing ulceration, the usual findings of chronic ulceration will be present except that the ulcer will be more shallow and more irregular in outline than in benign peptic ulcer. Occasionally the luetic ulceration will extend as deep as the peptic ulcer.

The chief value in the microscopic examination is in excluding the presence of a neoplasm or some other specific pathology, and one must not expect the pathologist to confirm the diagnosis from the slides alone as it rarely can be done, and one must not be deterred from making a diagnosis of syphilis of the stomach, provided he has sufficient evidence, by the lack of this confirmation.

The macroscopic findings are much more typical of syphilitic involvement of the stomach than are the microscopic findings, and in most cases the macroscopic findings will be sufficiently typical to make, or strongly suggest, the correct diagnosis. For this reason the surgeon should be familiar with the gross pathology so that he may recognize it at the operating table. Meyer and Singer<sup>19</sup> have given a detailed description of the findings at operation, and for those interested a thorough study of their article is suggested. For a brief description of these findings I will quote some of their comment and summary as follows:

The responsibility of recognizing the presence of syphilis of the stomach logically falls on the surgeon. The features that serve to distinguish syphilis of the stomach from carcinoma, which is most closely simulated, are as follows: there is a striking disparity in many cases between the extent of the lesion as determined roentgenologically and the extent as observed operatively by palpation. Whereas in carcinoma one generally finds at laparotomy a more extensive involvement than the X-ray picture indicates, in syphilis of the stomach there is a surprising paucity or complete absence of changes as determined by palpation. The common lesion of gastric syphilis is not a spherical prominence as

in a tumor, gummatous or neoplastic, but is a flat infiltrate that leads to a plaque-like thickening of the gastric wall. When thin, the infiltrate is readily overlooked. When thick, its relatively soft consistency and pliability distinguish it from carcinoma. On cross section the increase is seen to be due to an edematous fibrous tissue located chiefly in the submucosa. Inspection of the interior of the stomach generally discloses one or more superficial serpiginous ulcers involving a large plateau formed by the infiltrate. The base of the syphilitic ulcer, contrary to the peptic variety, is situated at a higher level than the normal mucous membrane. Fibrous and edematous thickening of the serosa and adhesions, when present, suggest an inflammatory rather than a neoplastic lesion. Associated syphilitic changes that may be detected during the course of the operation include hepatic, intestinal and splenic syphilis. Of these, the co-existence in the liver of gummas, deep stellate scars or sub-total destruction of the left lobe is of greatest aid in the recognition of the type of gastric disease present.

#### ROENTGEN FINDINGS

As the roentgen findings of syphilis of the stomach have been described fully by Moore and Aurelius,<sup>20</sup> and others, only a brief review of them will be given here.

Three varieties of syphilitic involvement of the stomach have been described: (1) gastritis; (2) ulcer, and (3) gummatous hyperplasia. Syphilitic gastritis may occur during the secondary stage of the disease but cannot be detected roentgenologically. It has been claimed that many simple round gastric ulcers are due to syphilis but this lacks confirmation. Practically all of the reported cases of syphilis of the stomach fall into the third variety: diffuse gummatous infiltration and fibrosis with thickening and contraction of the gastric wall. The mucosa over the involved area frequently shows single or multiple shallow irregular ulcerations. Occasionally the ulcerations may extend very deep and may even perforate.

The location of the area of involvement has been given by Moore and Aurelius<sup>20</sup> as prepyloric 70 per cent, median or hourglass 22 per cent and, diffuse 8 per cent.

In the median or hour-glass type the prepyloric and the cardiac portions are uninvolved and the lesion is situated in the middle third of the stomach. In this type there is a smooth annular constriction which will give an hour-glass defect, or more commonly the defect will be more extensive so that it assumes a dumb-bell shape more than an hour-glass. A notable feature in most of the cases is the great length of this constriction in contradistinction to the typical hour-glass deformity seen associated with benign gastric ulcer. The typical hour-glass defect may, however, be seen in some cases due to syphilis. Instead of having an annular constriction as described above there may be involvement of only the greater curvature of the stomach. This will be well shown in the case which I will report. There may be a relatively smooth filling defect involving the greater curvature in the middle third of the stomach and there may be an ulceration in this filling defect (Fig. 1).

In the prepyloric type, almost without exception, the defect in gastric contour is concentric and rather symmetrical. The contraction is usually pronounced with the lumen narrowed progressively toward the pylorus resulting in a spicular form of the barium shadow, but in some cases it is of tubular shape with constant dimensions. Regardless of the length of the defect, the lumen pursues a straight, or fairly direct course in contradistinction to the markedly tortuous course usually found in carcinoma.

Only 8 per cent of the cases fall into the third group with such diffuse involvement that little remains of the stomach. In reality, I believe that this group is merely the end stage of the prepyloric group and that if a case of the prepyloric group remains untreated it will progress until the entire stomach will become involved, resulting in marked contraction and diminution in size. The transition from the prepyloric to the diffuse is well shown in my case (Figs. 2 and 3). In all cases the contraction is obvious but varies in degree

with some so extensive that only a narrow smooth canal is left, with the cardia reduced to a very small pouch. In this type the barium column may show some delay in entering the stomach and the lower esophagus will show some dilatation due to this, but the esophagus itself is practically never involved by extension of the process from the stomach. The barium passes very rapidly through the stomach and, due to the gaping pylorus, the duodenal cap will appear to be larger than normal, but this is more apparent than real.

If an ulceration is present, the niche will usually not penetrate beyond the normal limit of the gastric lumen as it does with benign gastric ulcer, but will be seen to involve the filling defect in a manner similar to that seen in an ulcerating carcinoma. Peristalsis is absent in the involved area and is seldom seen in the uninvolved areas. The gastric rugae are obliterated and the gastric wall is less pliable than normal on palpation. If a tumor can be palpated it usually will be much less prominent than the size of the filling defect would indicate, and this is a very important point in differentiating between syphilis and carcinoma of the stomach. This absence of a palpable mass, notwithstanding the presence of a gross and constant filling defect, has been emphasized more than any other sign and merits the stress it has received.

Following antisyphilitic therapy it may be seen that the lesion will completely disappear, but on subsequent examination at a later date the filling defect may be seen to have recurred due to scar tissue formation as a result of the healing process. In many other cases, and in all cases showing extensive involvement, no change will be noted in the roentgenological findings in spite of pronounced clinical improvement.

## DIAGNOSIS

There are no pathognomonic findings in syphilis of the stomach. The diagnosis must be made by a consideration of all

available data. Many rules have been laid down in the literature as requirements which must be fulfilled before a diagnosis can be made, but in no case will all of these requirements be found. No set rules can be laid down for the diagnosis of the disease. Usually the hardest part in making the diagnosis is to consider the possibility of the presence of a syphilitic lesion in the stomach. Of course, the diagnosis of syphilis of the stomach cannot be made if the possibility of the disease is not considered. Once the possibility is considered, the diagnosis will not prove to be very difficult after consideration of all of the data. The surgeon can frequently make the diagnosis at the operating table; the roentgenologist can make the diagnosis in many cases, especially if he considers the obvious clinical differences between patients with carcinoma and those with syphilis, and in many other cases he will render valuable aid to the clinician by suggesting the possibility of syphilis; the pathologist can practically never make the diagnosis just from histological examination.

Eusterman and Balfour<sup>9</sup> assert that "in all cases of syphilis in which a demonstrable gastric lesion is present, regardless of the roentgenologic type or extent of the lesion, the condition should be regarded as syphilitic until it is proved to be otherwise."

The typical patient with gastric cancer is beyond forty years of age, looks gravely ill, is cachectic and has a palpable tumor corresponding in size and location to the roentgenologic deformity. The typical patient with gastris syphilis is less than forty, is thin but not weak or markedly ill, is not cachectic and has no palpable tumor mass in relation to the filling defect. Symmetrical narrowing of the prepyloric segment without a palpable tumor should always suggest the possibility of syphilis. The disease is to be considered when a patient has a lesion resembling scirrhous carcinoma, but is relatively young.

## TREATMENT

Antisyphilitic treatment should instituted immediately in all cases except those with marked obstructive symptoms which demand immediate surgical relief. In all cases of dumb-bell constriction there will probably be so much scar tissue present that antisyphilitic treatment will cause no anatomic restoration and these cases must be treated surgically. In many cases antisyphilitic treatment will cause a disappearance of the gastric lesion with a return to normal in gastric contour. In some of these cases, even though there may have been complete anatomic restoration, there may later develop obstruction due to scar tissue formation and these patients will then have to be treated surgically for relief from the obstruction.

#### CASE REPORT

R. W., white male, aged sixty-two, was referred to the hospital for roentgen examination of the stomach, by Dr. S. W. Mooring.

His family and past histories are relatively unimportant.

About one year previous to his coming to this hospital he began to have attacks of pain in the abdomen. These attacks rapidly grew worse and at times were severe enough to necessitate his leaving his work and going to bed for an entire day. At other times the pain was less severe and of shorter duration. He vomited occasionally at first and this rapidly increased in severity until he began to vomit practically everything that was eaten. There was no relation between eating and the vomiting. There was a rapid loss of weight. His average weight at the onset of his illness was 158 pounds. At the end of six months his weight was 145 pounds. At this time (August, 1932), he consulted the physicians in another hospital and a roentgen examination of his stomach was performed. This examination revealed a smooth filling defect on the greater curvature of the stomach with its lower margin about 3 inches from the pylorus (Fig. 1). In the center of this defect there was a definite ulceration, but this ulceration did not extend beyond the normal limit of the gastric outline. No mass could be palpated. A diagnosis of carcinoma of the stomach was made and he was advised to undergo an operation, but this he refused.



Fig. 1. August 2, 1932. Note filling defect, with ulceration, on the greater curvature of the stomach.

The vomiting continued and he continued to lose weight. He continued to eat solid foods but by now this always caused vomiting and he put himself on a diet of raw eggs and goat's milk.

He was re-examined at the same hospital on April 12, 1933, eight months after the original examination. Ten days after this examination he consulted his physician in this city and was referred to this hospital for roentgen examination. This revealed that the filling defect, seen at the first examination, had disappeared but there was a constant narrowing of the lower third of the stomach. Peristalsis did not pass over this area. There was a smooth defect on the greater curvature in the middle third of the stomach and from this defect small, smooth projections could be seen to extend beyond the limit of the defect (Fig. 2). No mass could be palapted. I felt that the lesion was very atypical of carcinoma and requested a re-examination after one week. This re-examination confirmed the previous findings and I finally concluded that it was a carcinoma. I did not consider syphilis, although the picture was very typical of this disease. At that time I also did not have the films available which were taken at the oth-



Fig. 2. April 12, 1933. The diffuse narrowing of the lower half of the stomach is well shown. The duodenal cap is not shown on this film. The irregularity on the greater curvature in the middle third is very atypical of carcinoma.

er hospital and had no way in which to make a comparison with his previous findings. Operation was advised and again was refused by the patient. He continued to lose weight but continued to work until August, 1933, at which time he was retired on a pension.

There was very little change except for a continued loss of weight and in February, 1935 (three years after onset of the illness) he was admitted to this hospital where he remained twenty-four days and was discharged at his own request. No roentgen examination was done.

In January, 1936, he returned for roentgen examination. He had continued to lose weight and still vomited at times. His diet was entirely liquid and this he was forced to drink very slowly. Roentgen examination (Fig. 3) revealed a definite delay at the lower end of the esophagus with some dilatation of this part of the esophagus. The stomach was markedly contracted and shortened. The cardia was irregular in

shape. Peristalsis was absent. There was no palpable mass. No mucosal relief could be seen. The stomach emptied rapidly through the gaping pylorus. The channel through which the barium passed was rather smooth in outline. The duodenal cap filled quickly and appeared to be large, but actually it was of normal size although its diameter was definitely greater than that of the stomach. The condition was thought to be due to an extensive scirrhous carcinoma and no treatment was advised.

He was next observed in April, 1938 (almost six years after onset of symptoms), and roentgen examination revealed no appreciable change since the previous examination (Fig. 4). He had lost more weight, which now was only about 80 pounds. This represented a loss of about 75 pounds during his illness. Due to his good general condition, in spite of the great loss of weight, and in view of no change in the roentgen findings in the stonach, it was thought that the condition was due to syphilis instead of carcinoma. A Hinton test was then done and was reported as being strongly positive for

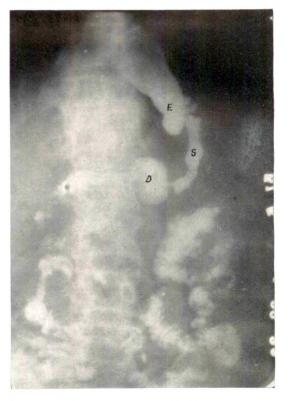


Fig. 3. January 22, 1936. The stomach shows extreme contraction. *E*, esophagus; *S*, stomach; and *D*, duodenum.

syphilis. He was to be given antisyphilitic treatment by his local physician but did not report to him for the treatments.

On December 19, 1938, he was brought to the hospital in an ambulance due to his weak condition. He was very emaciated. The urine examination was negative. The red blood count was 2,460,000 and the white blood count was 5,700. The hemoglobin was 46 per cent. Physical examination revealed a very emaciated man. The pupils reacted sluggishly to light and accommodation. No masses were palpable in the abdomen. No other abnormal finding was noted. Antisyphilitic treatment was started and continued during his stay in the hospital. He was discharged from the hospital on February 20, 1939. His general condition was greatly improved. He had gained 14 pounds in weight and was much stronger. The red blood count was 2,690,000 and the hemoglobin was 52 per cent.

He returned to his home and continued to receive antisyphilitic treatments.

In April, 1939, he returned for a re-examination of his stomach. He had continued to gain strength and weight and he now weighed 111



Fig. 4. April 9, 1938. No appreciable change since the previous examination.



Fig. 5. April 5, 1939. No change can be noted following antisyphilitic treatment. The apparent enlargement of the duodenal cap is well shown.

pounds (a gain of 31 pounds since beginning of the antisyphilitic treatment). His general condition was excellent. Roentgen examination revealed no change in the findings in the stomach (Fig. 5).

On August 17, 1939, he was re-admitted to the hospital in a very poor condition. He was semidelirious and no interval history could be obtained. He had lost much weight and he vomited practically everything that he took. He remained in this condition for five days, at which time an infection of one side of his face developed. This rapidly spread to the other side and he died on the seventh day following his admission. Through the strenuous efforts of Dr. E. F. Greene permission for a postmortem examination was granted.

The report of the postmortem examination, performed by Dr. F. L. Burnett of Boston, is as follows: The body is that of a prematurely old man who is greatly emaciated. The skin is clean, the subcutaneous fat greatly reduced,

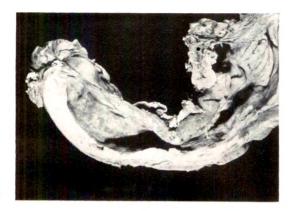


Fig. 6. August, 1939. The stomach is open showing the mucosa and the marked thickening of the gastric wall. The stomach measured 12 cm. in length and 5 cm. in its greatest width at postmortem examination.

but the muscle is of a good color. The omentum forms a thin veil over the abdominal contents. The stomach is very greatly reduced in size and measures 12 cm. in length and 5 cm. in its greatest width (Fig. 6). It is constricted in its mesial portion to form some diverticula. It has a capacity of about 65 cc. The wall is of a uniform thickness and measures about 5 to 6 mm. but forms some diverticula of 4 cc. capacity or less. The mucosa is slightly discolored, especially about the openings of the diverticula. Masses cannot be found in the intestinal walls. The liver does not appear reduced in size, but on the anterior surface there is a small, light colored area about I cm. in diameter. The markings are definite but the cut surface has a greenishbrown color. The gallbladder is free of stones and is filled with a thin, yellowish-green fluid. The pancreas, spleen, and adrenals do not appear abnormal. The pelves of the kidneys are dilated and the markings of the cortex are definite. There are firm fibrous adhesions at the apex of the left pleural cavity but the lung is soft. There is an area of consolidation in the posterior portion of the right lung. The heart is not enlarged, the muscle is of good color, and the valves are not abnormal. The aorta is not dilated and the intima is smooth. There are no masses in the mediastinum. Microscopic examination revealed no important findings in the organs exclusive of the stomach. No evidence of a malignant tumor could be found

The stomach was sent to the Department of Pathology of the Massachusetts General Hospital in Boston and the report of Dr. Benjamin Castleman is as follows: The microscopic examination shows scattered groups of lymphocytes and plasma cells, very often surrounding small vessels throughout the muscularis. In some areas between muscle fibers there are groups of epithelioid-like cells with giant cells. The findings are quite consistent with syphilis.

#### SUMMARY

Syphilitic involvement of the stomach occurs more frequently than is realized, although it is not a common finding.

The diagnosis is made only after consideration of all of the available data. It is most frequently mistaken for carcinoma and the failure to consider it as a possibility is very often the reason for an incorrect diagnosis. There are no pathognomonic findings.

The pathologist is unable to make the diagnosis in most cases and the value of this examination lies in excluding other pathology.

The clinical, pathological, gastroscopic, and roentgen findings are given and a case is reported showing the progressive changes from early to very extensive involvement of the stomach.

## REFERENCES

- Cabot Case Record No. 21182. New England J. Med., 1935, 212, 849.
- Cabot Case Record No. 23451. New England J. Med., 1937, 217, 787.
- CAREY, J. B., and YLVISAKER, R. S. Gastroscopic observations of syphilis of the stomach. *Ann. Int. Med*, 1938, 12, 544-550.
- 4. CARNS, M. L. Syphilis and carcinoma of the stomach. Wisconsin M. J., 1935, 35, 725.
- 5. Edie, E. B. Syphilis of the stomach. Penn ylvania M. J., 1933, 36, 586.
- Estes, W. L., Jr. Syphilis of the stomach. Am. J. Surg., 1933, 20, 366-377.
- Eusterman, G. B. Gastric syphilis; observations based on 93 cases. J. Am. M. Ass., 1931, 96, 173-179.
- 8. Eusterman, G. B. Personal communication, May, 1939.
- Eusterman, G. B., and Balfour, D. C. The Stomach and Duodenum. W. B. Saunders Co., Philadelphia, 1935.
- Finney, J. O. Syphilis of the stomach. South. M. J., 1937, 30, 1058-1062.
- GORDON, A. M. Syphilis vs. carcinoma of the stomach—thorium dioxide injection. J. Iowa M. Soc., 1936, 26, 674-676.

12. Gutzeit and Teitge. Quoted by Carey and Ylvisaker, ref. 3.

13. Hartwell, J. A. Syphilis of the stomach. *Ann. Surg.*, 1925, 81, 767–790.

Kaplan, B. A case of gastric syphilis simulating carcinoma of the stomach. New England J. Med., 1933, 209, 1270–1274.

15. LEWALD, L. T. Roentgen diagnosis of gastric syphilis. *J. Am. M. Ass.*, 1931, 96, 179–183.

16. MAYER, H. J. Syphilis of the stomach. Am. J. Digest. Dis. & Nutrition, 1937, 4, 503-507.

17. McNee, J. W. Syphilis of the stomach. *Quart. J. Med.*, 1922, *15*, 215–226.

 MERRILL, A. S. Syphilis of the stomach, with a study of ten probable cases. Am. J. ROENT-GENOL. & RAD. THERAPY, 1924, 12, 444-453.

 MEYER, K. A., and SINGER, H. A. Syphilis of the stomach. *Arch. Surg.*, 1933, 26, 443–464.

Moore, A. B., and Aurelius, J. R. Roentgenologic manifestations in 87 cases of gastric syphilis. Am. J. Roentgenol. & Rad. Therapy, 1928, 19, 425–432.

21. Moutier, F. Quoted by Carey and Ylvisaker, ref. 3.

22. Noguchi. Quoted by Pusch, ref. 26.

23. O'LEARY, P. A. Gastric syphilis; data accumulated from 89 cases. Am. J. Surg., 1931, 11, 286–293.

24. Priestley, J. T., and Walters, W. Indications for operation in gastric syphilis. Surg., Gynec. & Obst., 1934, 58, 1030-1035.

25. Pusch, L. C. Ulcerative syphilitic lesions of the stomach—pathological anatomy of 4 cases. *Virginia M. Monthly*, 1933, 60, 227–232.

26. Pusch, L. C. Syphilis of the stomach. *Internat. Clin.*, 1935, *1*, 56–67.

27. SINGER, H. A., and DYAS, F. G. Syphilis of the stomach. *Arch. Int. Med.*, 1928, 42, 718–734.

SPROULL, J. Discussion of the occurrence of benign ulcer on the greater curvature. Am. J. ROENTGENOL. & RAD. THERAPY, 1931, 25, 464-473.

Vest, W. E. Gastric syphilis. West Virginia M.
 Ĵ., 1933, 29, 249–256.

30. Widen, A. Case of visceral syphilis operated upon twice—with an interval of 26 years—because of a suspected cancer of the stomach.

Acta dermat.-venereol., 1937, 18, 216-223.

31. WILLIAMS, C. Syphilis of the gastrointestinal tract. Am. J. Surg., 1934, 24, 834–853.

# DISCUSSION OF PAPERS BY DRS. LAING, WEBER AND BARGEN, WALTERS, DOUB, AND MCPEAK

Dr. H. E. Mock, Chicago. First I want to thank all the essayists for sending their papers to me, but I was told that I was to limit my discussion to Dr. Walters' paper only. There is so

much meat in his paper that I hate to turn to the criticism of it, on which I wish to speak from the standpoint of too much operation of gastric ulcers.

First I should like to show some slides to emphasize what he said about papillomata. (Slide) This small one was diagnosed by Dr. J. Sagel, at Methodist Hospital, Gary. On the surface when I operated was this bleeding area accounting for the marked anemia that the man had. The pathologist pointed out to me that this might undergo sarcomatous degeneration. It is four years now and there are no signs of it yet.

(Slides) The next one is a very large fibropapilloma. The first one was on the greater curvature and, as you see, this is on the lesser curvature. It was removed by the transgastric route, a rather wide base taken off, and the posterior wall repaired. The pathologist here called it benign. One year later this patient went to another hospital in Chicago and a diagnosis of carcinoma was made without any biopsy, but I think she has metastatic sarcoma from this papilloma, a condition that we must bear in mind in these papillomata.

I want to add my opinion concerning the operability of carcinomas. I think that every lesion of the stomach diagnosed as carcinoma should be explored and, as Dr. Walters says, the removal of many of these inoperable carcinomas is worthy of great praise.

Twenty and thirty years ago a bitter battle waged between Sippy and his followers and the surgeons of the country. Many of you remember those famous meetings when they would argue over this subject of gastric ulcers, and the internists won out to the point that most of us were swayed over at least to try the medical management of these lesions.

Dr. Walters refers to this period when he states: "Unfortunately a wave of enthusiasm to advise medical treatment in all cases in which a roentgenological diagnosis of gastric ulcer was made led to the postponing of necessary operations." Personally, I think this was a very fortunate wave of enthusiasm and one which has been wholeheartedly accepted by the majority of the surgeons of the country. During these thirty years literally hundreds of thousands of patients have received medical treatment for gastric and duodenal ulcers. I dare say in this audience there are at least ten who have had treatment for ulcers. Many of these patients had the benefit of excellent roentgeno-

logical diagnosis and really had the ulcers, but a very high percentage were diagnosed on symptoms and clinical history alone or by very inadequate roentgen films and faulty interpretation of the same.

We must remember that the manufacturers' agents have been very active for more than thirty years in selling one or more roentgen-ray outfits in every community of the land. The supply of really competent roentgenologists for at least half of that time was very small and still is insufficient to cover the country. Unquestionably a high percentage of so-called ulcers were erroneously diagnosed and never existed. Medical treatment was not dangerous, but if wholesale surgery for these cases had become the rule one of the darkest chapters in the history of our profession would have been written.

No one has greater respect for the ability of Dr. Walters than I have. If I get a cancer, there is where I am going. However, I cannot agree with his premise that because 17 per cent of all gastric ulcers eventually become malignant, all ulcers should be resected either locally or by gastric resection. He implies this when he states: "At The Clinic we assume that every ulcerating lesion of the stomach is malignant until proven to be benign." If he had added "either by roentgen-ray, therapeutic test or those needing it by exploration," I would agree with him.

Tuesday, at the Wisconsin State Medical meeting, I heard another great authority state, "Any patient in the cancer age, who has digestive disturbances that do not readily yield to medical and dietary management should be explored and a biopsy diagnosis made."

I do not believe that any of us who teach surgery or any of you who teach roentgenology, whose opinions have great influence with the average surgeon or roentgenologist throughout the country, can afford to take such a radical attitude toward the operative treatment of all ulcers.

An operative rate for gastric resections of 3.2 per cent, and even of 5.6 per cent as reported in another clinic, is exceptional. Mortality rates of 11 per cent or more have been reported. It will be much higher than this in the hands of the occasional operator; therefore, I feel that the death rate from needless surgery on benign ulcers would probably be far greater than the number saved by the early discovery of cancer in even 20 per cent of the ulcers.

What are the facts, not in the great clinics of the country where the more serious cases naturally drift, but out in the field where people in every walk of life depend upon local facilities? Let us take a very large city and an average size city for examples. Dr. Jacob Sagel, of the Methodist Hospital in Gary, told me that whereas he diagnoses many gastric and duodenal ulcers in the course of a year and whereas he has succeeded in having the management and course of the ulcer carefully followed and rechecked by roentgen examination, yet he is positive that not more than 3 per cent of the cases studied have been diagnosed as or proved to be malignant. He lives with his doctors and his patients and would soon know if he were missing 6.5 per cent of gastric cancers.

Dr. Clarence F. G. Brown has been in charge of the gastrointestinal clinic at St. Luke's Hospital for fifteen years. The Sunday morning follow-up dispensary run by this clinic averages 80 to 100 patients. Full roentgenologic facilities are afforded by Dr. Jenkinson. He states, "In a long-time observation in our clinic (fifteen years) only 3 to 4 per cent of the gastric lesions are or become malignant. This amounts to about the same end-result as routine universal operation and the individual lives longer and less expensively without surgery."

In every other respect Dr Walters' paper is a milestone and a guide in the management of gastric malignancies. Internists, surgeons and roentgenologists must cooperate to secure better diagnosis and better follow-up of gastric ulcers. If symptoms persist after adequate medical management of six weeks, the roentgen study should be repeated. As long as evidence of the ulcer exists it should be rechecked every six months and if, in spite of treatment, it shows signs of increasing in size or deformity, it should be explored. Every gastric cancer should be explored for many may prove to be operable, or a benign granuloma may be found which careful biopsy alone can differentiate from a cancer.

Finally, I wish to reëmphasize what Dr. Walters has stated concerning fibropapillomata of the stomach. They are silent bleeders often. They are easily overlooked. They tend in time to undergo sarcomatous changes.

Dr. B. R. Kirklin, Rochester, Minn. All roentgenologists will share my gratification at Dr. Laing's and Dr. Walters' high appraisal of roentgen examination for the diagnosis of gas-

tric disease. Whether the roentgenologist shall have an opportunity to examine the patient who has a gastric lesion rests on the clinician as a primary responsibility. When this opportunity is granted, a great share of responsibility for disclosing and identifying the lesion is transferred to the roentgenologist, and I am glad to hear the in the estimation of others he is adequately fulfilling his duty. Likewise, I believe that all roentgenologists will heartily approve and appreciate Dr. Walters' warning that roentgenologic methods, or rather those who apply them, are not infallible. Roentgenologists themselves have repeatedly stressed this fact and welcome its reiteration. By directing attention to three similar diagnostic errors that occurred at the Clinic last year Dr. Walters has again shown that occasionally prepyloric cancer can be confounded with duodenal ulcer by the roentgenologist. With interest stimulated by his paper, I have canvassed the statistics of the Section on Roentgenology of the Clinic for the entire year of 1938, and I believe these figures are fairly representative of the results obtained by most roentgenologists. During that year 229 patients, all of whom had been examined roentgenologically, were found at operation to have gastric cancer. Positive report that a lesion existed was made in 225 cases, or 98.3 per cent. In 4 cases the roentgenologist failed to discern any lesion. In 184 cases (80 per cent) the disease was definitely diagnosed as cancer. To these may be added II cases in which the lesion was suspected to be malignant and so reported, so that 85 per cent accuracy may reasonably be claimed. In no instance in which the roentgenologic diagnosis was cancer did cancer fail to be found. Among 31 cases in which cancer was not named specifically, the diagnosis was, variously, diffuse hypertrophic gastritis (in a stomach that had been resected), polyp or polyps, ulcer, ulcerating lesion, and lesion at the outlet with or without obstruction. Added to these were the 3 cases diagnosed as duodenal ulcer. I feel that few of these errors or incomplete diagnoses were culpable. Although apparently benign polyps usually are partly malignant the fact can be determined only by microscopic examination. Occasionally ulcers that appear both roentgenologically and macroscopically to be benign, prove to be malignant. The roentgenologic differential diagnosis of lesions near the pylorus is notoriously difficult, as Dr. Doub has pointed out so clearly, and often it is wiser to refrain

from attempting to predict their exact nature. The diagnosis of hypertrophic gastritis and those of duodenal ulcer were misleading, and as roentgenologists are human they will probably continue to make such errors occasionally. Certainly it is sometimes impossible to determine accurately whether a lesion is on the duodenal or the gastriz side of the pylorus, and clinicians as well as roentgenologists should be keenly conscious of the fact.

My own experience conforms with Dr. Doub's conclusion that ulcers in the prepyloric segment, like those on the posterior wall or greater curvature, are more likely to prove malignant than ulcers situated elsewhere in the stomach.

With Dr. McPeak I agree heartily that there are no pathognomonic roentgenologic signs of gastric syphilis, and that the diagnosis must rest on a correlation of all available evidence. At best the ciagnosis is precarious, for often it is almost impossible to distinguish gastric syphilis from scirrhous carcinoma, and I feel that, even when the pazient is known to be syphilitic, surgical exploration of his gastric lesion should not be delayed too long by therapeutic tests to determine the character of the lesion.

DR. WALTERS (closing). I am particularly glad to have had Dr. Mock mention the disadvantages of the viewpoint that all patients who have gastric ulcers should be operated on. Such was not my intent in the paragraph in my paper in which I said that at the Clinic we regard all gastric ulcers as being malignant until they are proved otherwise, that is, until proved to be benign.

Now what methods are there of proving that a "gastric u cer" diagnosed roentgenologically is benign or malignant? There are none. Disappearance of the niche from the roentgenogram or on fluoroscopic examination can be accomplished by invasion of the base of the ulcer by the carcinomatous process, as Schindler has demonstrated gastroscopically. Time and again I have seen patients who seemed to have benign gastric ulcers, which at operation were found to be alcerating carcinomas. In some of these cases under medical treatment the niche has disappeared from view roentgenologically, symptoms have subsided and blood has disappeared from the stool, but the patient has been operated on later and carcinoma of the stomach found at the site of the seemingly benign

If we are going to improve our results, in the

treatment of carcinoma of the stomach (I state it this way because the surgeon and the internist are dependent on the roentgenologist to identify the site of the lesion), all must remember that the fluoroscopic appearance of a benign gastric ulcer does not always exclude its being an ulcerating carcinoma. Until the time arrives when roentgenologic data are available to make the differential diagnosis which will prove the ulcer benign, all should accept the viewpoint that an ulcer of the stomach may be malignant.

When the ulcer is small, the symptoms are of short duration and the patient is young, certainly no surgeon with any knowledge of gastric pathology and gastric surgery is going to advise an operation without every attempt being made to heal the lesion medically. Furthermore, the conscientious surgeon is not going to operate on the large group of patients who have medium-sized gastric ulcers without the complications of hemorrhage or perforation and who have never been given the benefit of a trial of a medical regimen. At the Clinic, patients who do not have such complicating factors are put in the hospital on a medical regimen for three

weeks. If at the end of that time the ulcer has disappeared, the symptoms have disappeared, and the blood has disappeared from the stool, the patient is permitted to go home, but he is instructed that he must be kept under the observation of his physician and mentgenologist and must have examinations of his so mach every three months for two years. This to exclude the possibility that the uncer instead of healing has been the site of an extension of the carcinomatous process in its border which has obliterated the crater of the v' is or that granulation tissue has only tempo. Ay filled in the crater of the ulcer. Should recurrence of the ulcer take place surgical removal should be advised.

The most important thing that I can bring to the roentgenologist is first a plea for the earlier recognition of malignant gastric lesions, some of which begin in polyps, others in ulcars or lesions which look like ulcers and which may be carcinomas and second that the roentgenographic report of "gastric ulcer" does not exclude the possibility that the lesion may be malignant.



# ANEURYSMS OF THE ASCENDING AORTA, AORTIC ARCH AND INNOMINATE ARTERY\*

A CLINICAL, ANATOMICAL AND ROENTGENOLOGICAL STUDY

By CHARLES F. NICHOLS, M.D., HERMAN W. OSTRUM, M.D., and BERNARD P. WIDMANN, M.D.

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URING the past few years, we have been impressed by the frequency with which at crysms of the aorta are either overlooke, or confused with other chest pathology. The most frequent errors in diagnosis are those concerned with pulmonary tuberculosis, asthma, chronic bronchitis, congestive heart failure, mediastinal neoplasm, pleurisy, angina pectoris, and carcinoma of the esophagus. From a purely clinical standpoint, it is easy to appreciate why such errors arise, since these conditions may produce symptoms similar to those caused by aneurysms of the aorta. We have felt that every suspected chest condition, from whatever cause, should be subjected to careful roentgenoscopic and roentgenologic study and that this closer cooperation between clinician and roentgenologist, where the roentgenologist acts in a consulting capacity, will result in more accurate diagnosis.

It would be well to emphasize that not all aneurysms of the aorta are accessible o roentgen study. The exceptions are represented by the type arising from the sinuses of Valsalva, but even these, as we have pointed out, have certain roentgenological characteristics which should at least raise a suspicion of their presence if the condition is an obscure one involving the root of the aorta. Another type of aneurysm which gives considerable difficulty is the small pouch type which develops either from the convexity of the arch and points in a cephalic direction or from the concavity of the arch and points in a caudal direction. Even here the roentgenologist may be of great assistance.

Aneurysms of the aorta may be divided into intrapericardial, sometimes called "an-

eurysms of symptoms"; and extracardiac, often called "aneurysms of physical signs." Those of the intrapericardial type involve the sinuses of Valsalva and are of-. ten prone to rupture before manifesting marked physical signs, unless complicated by a ortic regurgitation; then the symptoms are those of syphilitic aortitis and the two offer considerable difficulty in differential diagnosis. The extracardiac type of aneurysm might well be considered as a space-taking intrathoracic lesion, and, since these aneurysms usually displace and compress neighboring anatomical structures, they nearly always produce definite physical signs. The clinical findings, however, in many of our cases were not so definite or reliable as the literature might lead one to believe. In fact, we believe that there are no classical pathognomonic symptoms and physical signs of aortic aneurysms and, while the diagnosis is very often clinically correct, the services of the roentgenologist are of inestimable aid in confirming or ruling out the presence of such a lesion:

In this study, we shall include aneurysms of the innominate artery because, from our experience, we believe that these aneurysms involve the arch of the aorta in their destructive process just as aneurysms arising from the posterior or the posterior portions of the arch tend to involve the orifice of the innominate artery in their destructive process.

While a few aneurysms of the aorta may be caused by atherosclerosis, mycotic implantation and other ill-defined infections, it is the consensus of students of the subject that at least 95 per cent of these lesions arise directly from syphilitic aortitis,

<sup>\*</sup> From the Departments of Radiology, Cardiology, and Medicine, Philadelphia General Hospital.

and our discussion will be confined to this group.

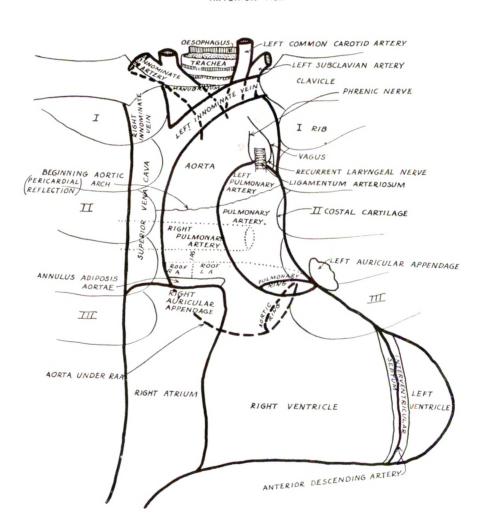
# ANEURYSMS OF THE ASCENDING AORTA

Aneurysms of the initial or the intracardiac portion of the ascending aorta produce perplexing physical signs, and roentgenological findings and in the past have received scant consideration. Their anatomical relations are complex and have been fully covered in our previous communication. We offer here a slightly different classification of aneurysms of the ascending aorta and the aortic arch.

A. Intrapericardial aneuty sms: These intracardiac aneutysms, annurysms of the aortic sinuses, or the sinuses of Valsalva, occur just above the aortic ring and are located at the proximal 1.5 cm. of the ascending aorta.

ASCENDING AND ARCH OF AORTA AND RELATED STRUCTURES

ANTERIOR VIEW



ROOF RA - ROOF RIGHT ATRIUM ROOF LA - ROOF LEFT ATRIUM I AS - INTERATRIAL SEPTUM

B. Extracardiac aneurysms: These involve the distal 4.5 cm. of the ascending aorta, which ends at the pericardial reflection. The physical signs and symptoms are dependent on the relation to the intrapericardial and the extrapericardial neighboring structures. Rupture would produce a hemopericardium.

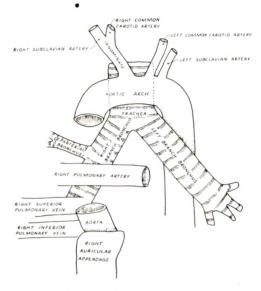
Clinical Anatomical Relations. Figures 1 and 2, showing the ascending aorta and the aortic arch, have been prepared from our own dissections of many autopsy specimens, and reference to these is necessary for an understanding of what happens in aneurysms of this portion of the aorta. The blood vessels coming off directly from it are drawn with heavy lines. In front of these are the upper sternum and the chondrosternal junctions, indicated by light lines. Structures posterior to the aorta are shown by light dots. The termination of the ascending aorta and the beginning of the aortic arch are shown by a wavy line, marking the pericardial reflection.

The clinical anatomy may be better understood by dividing this portion of the aorta into the proximal and the terminal portions of the extracardiac aorta:

- A. The proximal portion of the extracardiac aorta is covered by the right auricular appendage, the underlying aorta being indicated by a brokendash line. To the right, on a posterior plane, is the superior vena cava. To the left is the aortic pulmonary septum, separating the aorta and the pulmonary artery. In front is the sternum in the region of the third chondrosternal articulation. Posteriorly, will be found from right to left the roof of the right atrium (R.A.), the upper border of the interatrial septum (I.A.S.), and the roof of the left atrium (L.A.).
- B. The terminal portion of the extracardiac aorta begins at the level of the upper border of the right auricular appendage, frequently indicated

FIGURE 2

TERMINAL PORTION OF ASCENDING AORTA CUT AWAY TO SHOW POSTERIOR RELATIONS

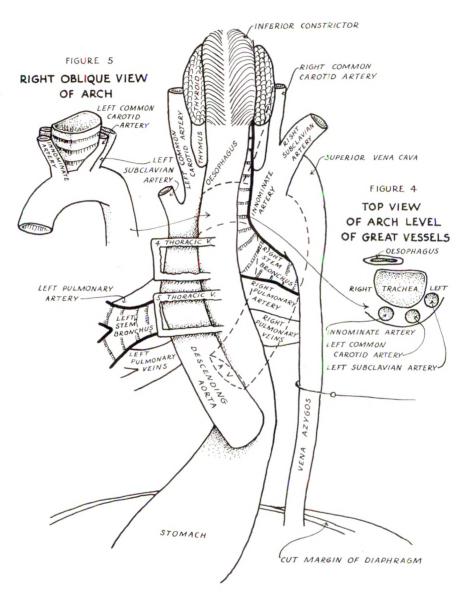


by a fatty ring on the anterior aorta, annulus adiposis aortae, which we have not found previously described. In Figure 2, this portion of the aorta is cut away to show the posterior relations, which are the structures entering into the formation of the root of the right lung. From below upwards, are the right pulmonary veins, the right pulmonary artery, and the right eparterial bronchus, respectively. In general, the ascending aorta is related: anteriorly, to the right half of the upper sternum; laterally, to the supracardiac vessels (superior vena cava and pulmonary artery); and, posteriorly, to the great transverse sinus and the structures entering into the hilum of the right lung.

# ANEURYSMS OF THE AORTIC ARCH

Clinical Anatomical Relations. In the consideration of these lesions, innominate artery aneurysms will be included and the terminal arch will be extended to include the beginning of the descending aorta which lies in front of the left half of the body of the fifth thoracic vertebra and behind the left stem bronchus. Figure 3 is a

POSTERIOR VIEW OF AORTA AND RELATED STRUCTURES



posterior view of the ascending aorta, the aortic arch, and the descending aorta. Broken-dash lines indicate the positions of the aortic valves, the aorta, and the great vessels lying in front of the trachea, the esophagus, and other organs. The vena azygos passing over the right bronchus is drawn aside by a hook. The components of the right and left lung roots are depicted, the ascending aorta passing in front of the

right root structures, and the terminal arch coursing behind the left root structures, respectively. The left halves of the bodies of the fourth and fifth vertebrae are fenestrated to show the terminal arch lying anteriorly.

The arch of the aorta lies in the superior mediastinum and is posterior to the lower part of the manubrium sterni. It commences at a point posterior to the right

border of the sternum, at the level of the second costal cartilage, and extends to the level of the lower border of the left side of the fifth thoracic vertebra. It has two curves, one with the concavity downward, and, what is more important clinically, a concavity posterior and to the left (Figs. I and 3). Anteriorly, it is related to the

(Fig. 1). Above, are the branches of the great vessels, whose origins are crossed by the left innominate vein (Fig. 1). Below, is the bifurcation of the pulmonary artery, the root of the left lung, the ligamentum arteriosum, and the left recurrent laryngeal nerve, lying between the aorta and the left pulmonary artery (Figs. 1 and 3).

# FIGURE 6 INNOMINATE ARTERY AND RELATIONS

(B) ANTERIOR VIEW (A) RIGHT LATERAL VIEW INTERNAL JUGULAR VEIN CAVERNOUS PLEXUS RIGHT COMMON CAROTID PLEXUS RECURRENT PHRENIC NERVE LARYNGEAL SUPERIOR NTERNAL CAROTID ARTERY NERVE CERVICAL SUBCLAVIA GANGLION ARTERY RIGHT VAGUS PHARYNGEAL PLEXUS EXTERNAL CAROTID PLEXUS THYROLD CARTILAGE MIDDLE CERVICAL GANGLION VERTEBRAL ARTERY TRACHEA INTERNAL MAMMARY ARTER INFERIOR CERVICAL GANGLION

mediastinal pleurae, the lungs, and the remains of the thymus gland. On the left side, it is crossed by the phrenic and the vagus nerves, and the recurrent laryngeal branch passes under the concave border just outside of the ligamentum arteriosum (Fig. 1). Posteriorly, and to the right, are the trachea, the left recurrent laryngeal nerve and the left border of the esophagus

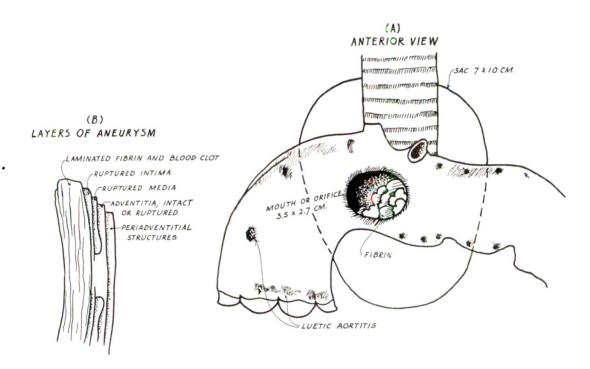
The Terminal Arch. It is recalled that the terminal arch is extended to the part of the aorta lying in front of the left half of the fifth thoracic vertebral body, so that this terminal portion of the arch has in front the left stem bronchus and behind the fifth vertebral body. Immediately preceding this, the aorta passes over the top of the root of the left lung, and behind it

is the left half of the fourth vertebral body. This terminal arch therefore practically embraces the left bronchus and is in relation to the left border of the esophagus, which lies anteriorly (Figs. 2 and 3).

In general, the transverse arch has a posterior concavity whose termination at the origin of the left subclavian artery is at a level or plane posterior to that of its

rior middle of the manubrium sterni to enc near the right sternoclavicular joint. It runs upwards and posterolaterally in the superior mediastinum. Its relations are as follows: posteriorly, it is in contact with the trachea; anteriorly, the left innominate vein courses in front of the orial of the artery; right laterally, it is in contact with the right innominate vein, the upper par

# FIGURE 7 ANEURYSM OF THE TRANSVERSE ARCH



commencement, just proximal to the origin of the innominate artery (Fig. 4). This concavity closely hugs the anterior and the left lateral trachea above the tracheal bifurcation (Fig. 4). The termination of the aortic arch is in intimate relation to the left stem bronchus, the left border of the esophagus, the left half of the bodies of the fourth and fifth thoracic vertebrae, and the left recurrent laryngeal nerve.

Innominate Artery (Figs. 1, 5 and 6). The innominate artery extends from the poste-

of the superior vena cava, and the right phrenic nerve; left laterally, at the lowelevel, is the left common carotid artery; a higher level, the trachea is in contawith it (Fig. 5). Posteriorly, at some ditance (Fig. 6 A and B) it is in relation the inferior cervical ganglion and the cevical sympathetic trunk. At its termin tion is the right recurrent laryngeal nerv

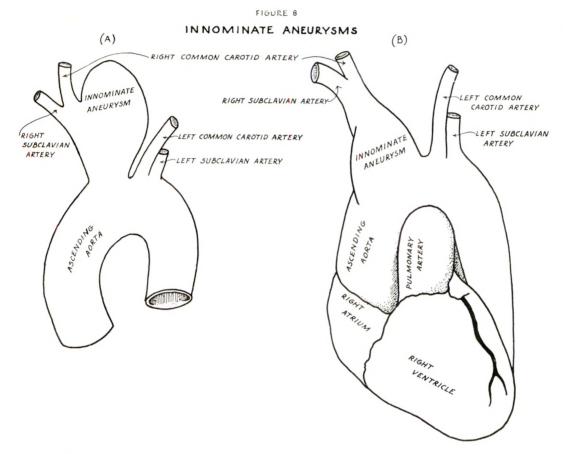
Clinical Pathology. The luetic proce produces a weakening of a diffuse segmen of the aortic walls, resulting in aneurysm



dilatations of two types: (a) Fusiform, which is produced by a diffuse luetic infiltration with thinning of the walls and intact arterial layers. It is infrequent in occurrence and runs a benign course without pressure phenomena. (b) Saccular (Fig. 7 A and 3), which is a luetic infiltration with thinning of a discrete portion of the aorta. This type may remain benign until

lar aneurysms occur more frequently at the convex and posterior surfaces, because these parts • are subject to greater hydrostatic strain from the moving column of blood.

Figure 7A is a schematic diagram of an aneurysm of the transverse arch, saccular type, with ruptured walls. The mouth measures  $3.5\times2.7$  cm., and the sac  $7\times10$ 



rupture of the aortic wall takes place. Then, if situated near an important viscus such as the left bronchus, early pressure symptoms occur. Later there is more or less extension of the aneurysmal sac, the outer layer of which may be adventitial or periadventitial tissue. There are then produced adhesions to, and displacement of, important structures, fistulous openings into hollow viscera, and sudden large hemorrhages.

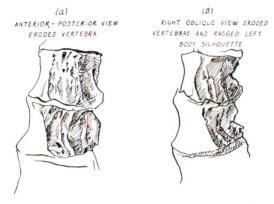
In the ascending aorta and arch, saccu-

cm. A cross section of the wall (Fig. 7B) shows, from within outwards, laminated fibrin and a blood clot, ruptured intima, ruptured media, intact or ruptured adventitia, and periadventitial structures. Dynamic pressure and displacement of structures, adhesions or fistulae to neighboring organs, depend on local anatomical relations and the extent of the aneurysmal sac. Figure 9, A and B, illustrates a frequent, important finding in aneurysms of the terminal arch; namely, an irregular erosion

and osteosclerosis of the left halves of the bodies of the fourth and fifth thoracic vertebrae. It is necessary to note that the erosion is best shown in silhouette in the right oblique position (Fig. 9B).

Figure 8,  $\mathcal{A}$  and  $\mathcal{B}$ , shows the two common types of innominate aneurysms of the distal and proximal portions. Infrequently the entire vessel or the median portion is

# FIGURE 9 EROSION OF FOURTH AND FIFTH THORACIC VERTEBRAE



involved. There are early pressure phenomena because of the small caliber of the superior mediastinum and of the important neighboring organs (Fig. 6 A and B).

Clinical Aspects. Detailed studies of the physical signs and symptoms produced by aneurysms of various portions of the aorta have appeared in the literature from time to time.2,3,4,5 We do not intend to explore all the possible signs and symptoms but rather to emphasize the anatomical relations of the aorta, and a knowledge of these relations, as shown in the accompanying illustrations, will serve to clarify and simplify the subject. Like all mass lesions in the chest, aneurysms give rise to what may be called general symptoms, more or less common to all types, and to symptoms tending to indicate the site of the lesion. Among the former, pain, cough, and dyspnea, are the most frequent. The special symptoms are peculiar to certain locations and result from pressure on certain vessels, nerves, or portions of the bronchial tree or esophagus.

It is well to remember that pain may result from pressure upon any structure within the thorax or upon the chest wall and, in the latter case, may be localized or may be segmental in distribution. Often, the pain is referred to both shoulders, both arms, the neck, the head, and the precordial area; but rarely to the back except when the terminal transverse arch or descending aorta is involved. Pain is possibly more frequent in the ascending group of aneurysms, but is common to all.

Pressure pain is usually associated with bone erosion and indicates that the aneurysm has reached the chest wall. Erosion of the ribs and sternum is usually less painful than erosion of the vertebrae but it should be emphasized that extensive erosion may occur without producing pain.

Cough is common to at least half of the group under consideration and is a manifestation of pressure upon the respiratory tract, causing irritation and deficient drainage. Any portion of the trachea, bronchi or lung, if irritated, produces a cough, with or without sputum. Hoarseness and a brassy cough occur in only a minority of cases and usually indicate transverse arch involvement, although the right laryngeal nerve may be irritated by an ascending arch aneurysm.

Dyspnea ranks high as an early symptom and may vary from a mild substernal oppression to the severe types, which resemble heart failure or asthma. Dyspnea is nearly always due to compression of the trachea, bronchi or lung. Dysphagia occurs in the transverse arch group, because here the esophagus may be intimately related to the lesion.

The physical signs and pressure phenomena which may be produced by aneurysmal sacs are numerous and often complex. Reference to the structures which may be pressed upon and to their anatomical relations will help to clarify the situation. Pointing of the aneurysmal sac may cause localized bulging and pulsations in the right or left upper chest, above the manubrium, above the clavicle, or in the

lower chest and back. Thrills and diastolic shocks are most numerous in the ascending and transverse arch groups, because of their anatomical accessibility. Cyanosis .. may occur in the ascending group from pressure on the superior vena cava, the pulmonary artery or the right auricle. Pressure upon the superior cervical sympathetic chain is probably responsible for the pupillary changes. The blood pressure and - pulse inequalities in the arms result from direct pressure upon the vessels leaving the arch, from loss of pressure in the vessels arising directly from the sac or from loss of pressure in the sac itself. Because of anatomical requirements for production, tracheal tug is found in less than half the cases. It may occur in both the ascending and transverse groups; in fact, any condition which anchors the left bronchus to the aorta may produce it. The heart is usually normal in size unless the aneurysm is complicated by a luetic aortic insufficiency or by hypertension. Humming murmurs may occur over the sac, but are uncommon, and are not an important finding. Pressure upon the trachea or bronchi produces lung findings such as lagging of respiration, bronchiectasis or even evidence of infection in the lower lobes. Heart failure is not a part of the picture in aneurysms unless complicated by aortic insufficiency or other conditions affecting the heart. For those who are interested in a detailed analysis of symptoms and signs resulting from various types of aneurysms, reference should be made to the excellent presentation of Kampmeier.5

An aneurysm of the innominate artery usually presents a more definite clinical course and picture than does an aneurysm of the aorta, and obviously much is known<sup>6,7</sup> about this variety because of its tendency to present in the neck. Reference to its anatomical relations, as shown in Figure 6, will clarify the physical signs and symptoms. Pain in the right shoulder, cough, and the presence of a pulsating tumor above the episternal notch, have been the most common findings in our

cases. This aneurysm tends to spread upward beneath the sternomastoid muscle and to compress and erode the sternum and clavicle; yet, having more space in which to spread, its symptoms usually become manifest later than do those of an aneurysm of the arch. In those cases where the arch of the aorta and the innominate are both involved, the tumor displaces the aorta, heart and trachea downward and to the left. In this type of aneurysm, there may occur venous congestion of the face (uncommon in our experience); cough, aphonia, and hoarseness from pressure on the right recurrent larvngeal nerve; changes in the pupils because of pressure on the sympathetic chain; pain referred to the arm, shoulder, head, or neck, from brachial or cervical plexus pressure; and dyspnea, as well as dysphagia, because of tracheal and esophageal pressure. Cough, dyspnea, and pain were by far the most common complaints.

### ROENTGENOLOGICAL DIAGNOSIS

Obviously, this is the most important • part of the examination, since size and location are thus accurately determined. In our experience, many aneurysms were first demonstrated by the roentgen ray, and changes in the lungs and related structures which clinically had been thought to be primary were thus shown to be secondary in nature. The aneurysms are usually much more dense than any of the surrounding structures, and the majority present smooth, rounded borders. Pulsations may be seen; but, in our experience, differentiation between expansile pulsations and motion transmitted from the heart has been impossible except in isolated instances. In fact, the great majority of aneurysms do not pulsate, because of disease in the wall, calcification, or the presence of a mural clot. All cases should be roentgenoscoped, since only in this way can a mass suggesting an aneurysm be separated from the great vessels, and the differentiation between a tumor and an aneurysm correctly made. In roentgenoscopic studies, pulsa-

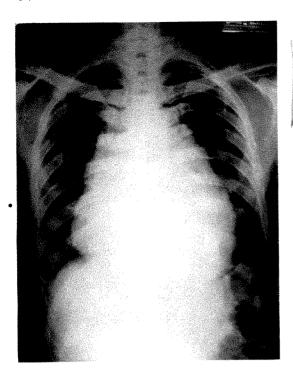


Fig. 10, Large fusiform aneurysm covering the entire heart shadow, no encroachment on the neighboring structures. The heart shadow is visualized through the fusiform aneurysm.

tions are best seen in the fusiform type (Fig. 10), in which there is usually an absence of blood clot and laminated fibrin. The pulsations are expansile in type, with a rapid expansion and a quick rebound of I the aortic shadow. In the saccular type, it is only in the early stages that we see expansile pulsations. After the formation of clots and laminated fibrin, fixation of the sac to the surrounding structures usually abolishes all expansile pulsations, and only transmitted movement is seen. Roentgenographic studies in the posteroanterior, lateral, and both oblique views offer the best means of clearly outlining the sac. The heart in the great majority of aneurysms of the aorta is not enlarged, and where enlargement occurs there is usually an aneurysm in the sinus portion of the aorta, causing aortic insufficiency. Syphilis of the aortic valve may be present in conjunction with an aneurysm higher along the arch. There is no physiological reason why a simple aneurysmal dilatation of the aorta should cause increased work for the heart. Very small saccular aneurysms are difficult to detect anywhere. Those in the heart mass, and smaller ones arising from the mid-portion of the convex and concave. portions of the aortic arch, are particularly hard to detect. However, a careful study of the trachea, the esophagus, the bifurcation, and the right and left main stem bronchi, is often helpful in detecting an aneurysm even in these locations, either because of encroachment on the lumen of the trachea and the bronchi or because of compression or displacement of these structures. Fusiform aneurysms produce sharp oval or semicircular out-pouchings, well circumscribed and often delineated by atheromatous plaques, which extend into either the right or left lung field and may overshadow, but not obliterate, the right or left cardiac border. Saccular aneurysms produce sharply circumscribed oval or semicircular shadows, continuous with the heart border and often delineated by thin, dotted, calcified plaques just inside the outer border of the sac. They produce characteristic erosion in the anterior and the lateral surfaces of the bodies of the vertebrae (Fig. 9). Because the intervertebral discs resist the destructive process better than the bodies of the vertebrae, the portions of the bodies nearer the discs are very little involved, producing scaphoid erosion of the bodies with intact overhanging edges.

Aneurysms of the Ascending Aorta (Fig. 11). Saccular aneurysms of the ascending aorta, from the vasoatrial junction to the beginning of the horizontal arch, extend most often into the right lung field, obliterating the right cardiac borders and, if large enough, may displace the heart and the aorta to the left. They may also extend anteriorly, and here the sternum and the chondral portions of the anterior ribs may be eroded (Fig. 12). The lower portions of the trachea and the main bronchi are very seldom encroached upon unless the aneurysm is large enough to extend well backward, and then the lower portions

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of the trachea and the main bronchi are displaced backward. Aneurysms with small pedicles attached to the ascending aorta are not uncommon and may resemble lung

Aneurysms of the Aortic Arch and Innominate Artery. Here, besides the characteristic oval, circular, or semicircular shadow, continuous with the heart border, we have other important criteria. We might say that generally all aneurysms of the arch displace the trachea to the right except the innominate and those arising from the extreme anterior portion of the horizontal arch, in which the trachea, if the aneurysm is large enough, is displaced to the left. Those arising from the anterior twothirds of the arch displace the trachea backward (Figs. 13 and 14), as does also the innominate aneurysm; and those arising from the distal horizontal and descending aorta displace the trachea anteriorly. The esophagus, being a more posterior structure, is displaced to the right and anteriorly

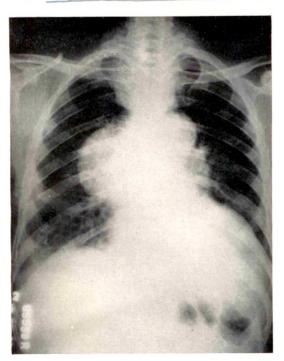


Fig. 11. Saccular aneurysm of the ascending aorta extending into the right lung field, obliterating the right cardiac border. Heart enlarged due to associated aortic insufficiency.

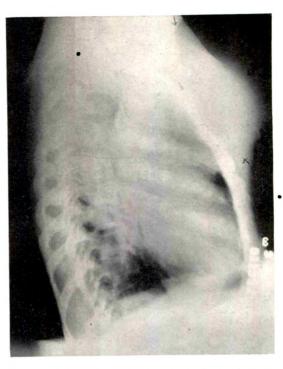


Fig. 12. Large saccular aneurysm destroying the manubrium, and anterior portion of the right first rib, protruding anteriorly beneath the skin, with subsequent rupture.

by aneurysms in the descending and distal portions of the arch. In other types, the aneurysm, if large enough, displaces the esophagus backward and to the left. The most common of all aneurysms we have encountered is the one arising from the distal, horizontal, and descending portions (Figs. 15 and 16). Here, in the posteroanterior view, the trachea and, to a lesser extent, the esophagus are displaced to the right; the left main bronchus is pushed downward and inward; and the lumen is narrowed. At times enough pressure is exerted on the lumen to produce atelectasis of the left lower lobe, and occasionally of the entire left lung, followed by infection and pleural effusion. When atelectasis or effusion occurs on the left side, the aneurysmal sac is entirely obscured and no indication of it will be seen on the roentgenogram (Figs. 17 and 18). However, in spite of the effusion and the atelectasis, which may cause a retraction of the heart to the left, the trachea is usually displaced (

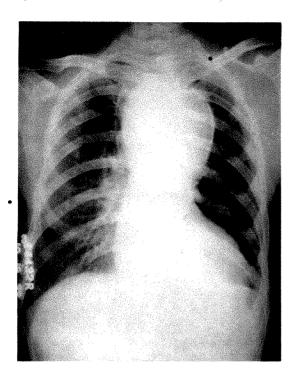


Fig. 13. Large saccular aneurysm with calcification of the sac, arising from the anterior two-thirds of the horizontal arch displacing the trachea to the right.

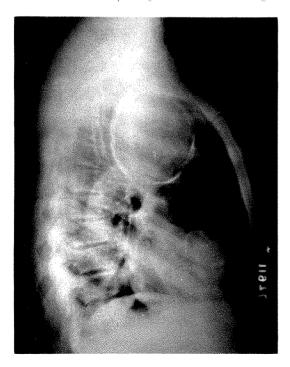


Fig. 14. Lateral view of Figure 13, showing the calcified aneurysm displacing the trachea backward and producing early erosion of the fourth and fifth dorsal vertebrae.

to the right in an arc-like fashion. A diagnostic pneumothorax, or removal of fluid with replacement by air, is a very important diagnostic measure. This type of aneurysm produces the typical anterior and lateral erosions of the dorsal vertebrae, previously described. We have observed several cases where the entire left half of the bodies of the fourth, fifth, and sixth dorsal vertebrae have been destroyed

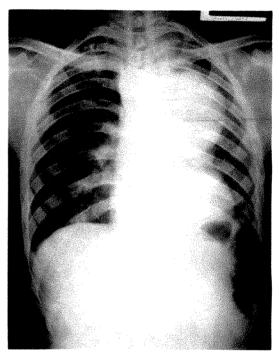


Fig. 15. Saccular aneurysm arising from the distal, horizontal and descending aorta, displacing the trachea and esophagus to the right. Heart not enlarged.

by the aneurysm (Fig. 19). To differentiate an aneurysm of the distal, horizontal, and descending aorta from diffuse dilatation, we must remember that in a true saccular aneurysm, because of the presence of laminated clots and fibrin, the density is greater than that of the heart mass, and the heart and the remainder of the aorta cannot be visualized through the aneurysm in the posteroanterior view. In the lateral view, the aortic knob is replaced by the sac. In the left anterior oblique, the sac is seen to encroach on the posterior portion of the

aortic window, and the trachea, as well as the esophagus, is narrowed and displaced to the right and anteriorly.

An aneurysm arising from the proximal portion of the innominate artery will produce a widening of the superior mediastinum (Fig. 20). The outer border is usually well-defined and straight, though sometimes oval in outline. It extends upward and to the right and fades into the neck



Fig. 16. Lateral view showing erosion of the fourth, fifth and sixth dorsal vertebrae, and anterior displacement of the trachea and esophagus by aneurysm arising from the distal, transverse and descending aorta.

tissue shadow. The inner border is usually obscured by the shadows of the spine and the mediastinum; but, when the sac is large enough, may be seen just to the left of these. When both borders are well visualized, the sac is shaped like a vase. The aortic knob is displaced downward and to the left; the trachea and the esophagus are displaced to the left and posteriorly; and the inner portion of the right clavicle, the manubrium, and the chondral portion of

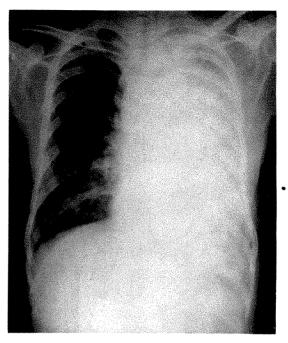


Fig. 17. Aneurysm of the distal, transverse and descending aorta with pressure on the left main bronchus and azygos veins, with atelectasis and effusion in the left lung.

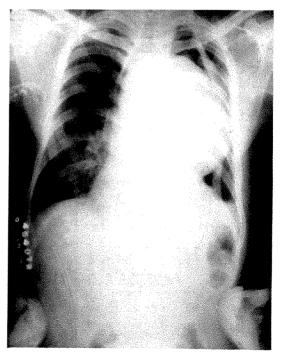


Fig. 18. After removal of fluid and introduction of air the large sac is visualized as well as the atelectatic left lung,

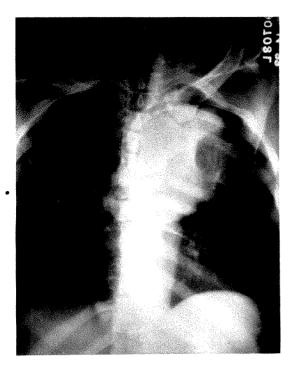


Fig. 19. Extensive destruction of the left half of the body of the fourth, fifth and sixth dorsal vertebrae and the approximating posterior ends of the fourth, fifth, sixth and seventh ribs.

the right first rib may be eroded. When the sacs are small, there is usually no involvement of the neighboring structures; when large, the right wall of the trachea is first encroached upon, the lumen narrowed and somewhat compressed, and the lower portion displaced to the left and somewhat tapered. An aneurysm in the extreme anterior portion of the arch will displace the trachea and esophagus in much the same manner as the innominate type, but an aneurysm in this region practically always involves the innominate artery.

Small aneurysms between the tracheocephalic vessels in the mid-portion of the arch may not encroach on the trachea or the esophagus. Aneurysms arising from the concave portion of the arch are more difficult to diagnose and visualize; but here, also, attention must be given to the lower portion of the trachea and its bifurcation, as well as to the right and left main bronchi. Aneurysms arising from the anterior portion of the concave arch will displace these structures posteriorly; and, conversely, those arising from the posterior portion of the concave arch will displace them anteriorly.

The differential diagnosis of mediastinal and lung tumors is at times difficult. An innominate aneurysm may resemble a tumor in the superior mediastinum, particularly a substernal thyroid. The latter, however, moves upon respiration, swallowing, or grunting, and the aortic arch is distinctly separated from it. An enlarged right lobe of the thyroid produces an archlike displacement of the trachea, with narrowing of the lumen, most marked in the region of the middle superior mediastinum. The left lobe of the thyroid displaces the trachea to the right. The lymphoblastoma group of tumors, such as Hodgkin's disease, lymphosarcoma, leukemia and thymoma, are usually situated in the anterior mediastinum, and the trachea is very seldom displaced laterally. If the tumor is large

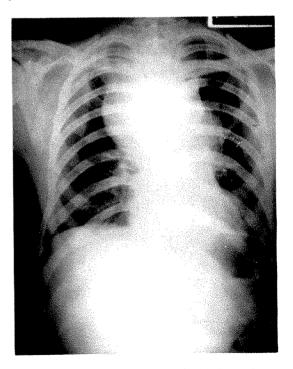


Fig. 20. Saccular aneurysm of the innominate, displacing the aortic knob downward and to the left and the trachea to the left and backward. The borders are sharply outlined, extending upward into the superior mediastinum.

enough, there may be a posterior displacement of the trachea. The aortic arch (with adequate films) can usually be separated from the mediastinal mass. These tumor ·masses are bilateral, enlarged in the vertical diameter, have indistinct outlines, and rarely show calcification. Mediastinal neurinomas may resemble an aneurysm, as they are usually fairly well outlined, unilateral, and may be dense enough to obscure the aortic arch. However, they affect the spine differently, produce a widening of the foramina and irregular erosion of the lateral portion of the bodies and the pedicles. At times, bronchogenic carcinoma may show a tumor mass not unlike an aneurysm. However, there is often some atelectasis, malignant lymphangitis, or tumor masses in the lung fields and, often, metastatic glands in the hilar and mediastinal regions. Loculated tuberculous pericarditis or other types of pericarditis may resemble aneurysms, but the size of the heart, absence of pulsations, clear lung fields, and other signs of pericarditis are usually present.

Prominence of the pulmonic salient as seen in pulmonary stenosis, interatrial septal defects, and patent ductus arteriosus. may also suggest an aneurysm. However, the markedly increased pulsations, as well as prominent and pulsating hilar vessels. together with right heart enlargement. usually make a differentiation possible. Aneurysmal dilatation of the left atrium, where the left atrium extends well over to the right, overriding the right atrial border, bears some resemblance to an aneurysm, but here the cardiac configuration is that of mitral stenosis and the lung fields show distention of the hilar and the perihilar vessels. Occasionally Pott's disease, with a mediastinal abscess, produces a bilateral

mediastinal tumor resembling an aneurysm, but a careful study of the spine and the aortic arch will easily differentiate it from an aneurysm.

#### CONCLUSION

Many articles dealing with aneurysms have been published but only a very limited number have been accompanied by anatomical studies. We have attempted in this presentation to emphasize the anatomical relation of the aorta and to show how a knowledge of this, as detailed in the accompanying illustrations, may serve to clarify and simplify the subject. Not only will this detailed anatomical relation be valuable in the diagnosis of aneurysms but it will also greatly aid in a differential diagnosis of all space-taking lesions which occur in the thorax, adjacent to the aorta.

We wish to express our appreciation of the cooperation and assistance of Dr. B. Robinson who has drawn the illustrations from his extensive autopsy studies.

#### REFERENCES

- OSTRUM, H. W., ROBINSON, B. D., NICHOLS, C. F., and WIDMANN, B. P. Aneurysms of aortic sinuses or sinus of Valsalva. Am. J. ROENTGENOL. & RAD. THERAPY, 1938, 40, 828– 837.
- HARE, H. A., and HOLDER, C. H. Some facts in regard to aneurysm of the aorta. Am. J. M. Sc., 1899, 118, 399.
- 3. Boyd, L. J. Study of four thousand reported cases of aneurysm of thoracic aorta. Am. J. M. Sc., 1924, 168, 654-668.
- 4. LUCKE, B., and REA, M. H. Studies on aneurysm. I. General statistical data on aneurysm. J. Am. M. Ass., 1921, 77, 935.
- KAMPMEIER, R. H. Saccular aneurysm of thoracic aorta; clinical study of 633 cases. Ann. Int. Med., 1938, 12, 624-651.
- 6. Warfield, C. H. Roentgen diagnosis of aneurysms of innominate artery. Am. J. Roentgenol. & Rad. Therapy, 1935, 33, 350-358.
- 7. Parks, H. Aneurysm of innominate artery. Arch. Int. Med., 1938, 61, 898-909.



# THE ROENTGENOLOGICAL DEMONSTRATION OF THE TRUE ARTICULAR SPACE

# WITH PARTICULAR REFERENCE TO THE KNEE JOINT AND THE INTERNAL SEMILUNAR CARTILAGE\*

By WILLIAM A. EVANS, JR. DETROIT, MICHIGAN

THE true articular space like the pleural space is a potential space which is visualized only under special conditions. A layer of articular cartilage covers the end of each bone at a diarthrodial joint and the two layers are ordinarily in close approximation to each other separated only by a thin layer of fluid. These two cartilages are normally represented by a uniformly radiolucent space between the bones, and changes in the cartilage are commonly implied from variations in the width of this space. An increased space is taken to indicate swelling and edema of the cartilage as the result of injury or disease or to a separation of the cartilages from an increased amount of articular fluid, a loose body locked between the cartilages, or relaxation of the capsular ligaments. Narrowing of the space indicates degeneration or destruction of the cartilage and rarely there may also be calcification. These implications without more direct evidence generally suffice. The knee, however, offers a special case for there are not only the cartilaginous coverings of the tibia and femur, but also the two semilunar cartilages which are subject to injury and disease and which then may become a basis for serious disability. The clinical diagnosis of meniscus injuries is often difficult and inaccurate at best. Schaer,1 in a recent study, estimates the incidence of positive and negative errors in diagnosis in his clinic as 15 per cent and the diagnosis becomes, of course, more difficult and important in medicolegal and compensation cases. In recent injuries the roentgen examination has been chiefly of value in excluding involvement of the bone structure, although there may be evidence of effusion into the joint and perhaps an increase in the spacing at the site of the lesion. In old cases there may

be demineralization of the bone structure about the affected knee with either an increase or decrease of the spacing between the tibia and femur on the side of the cartilage injury. Frequently we have also noted a localized sclerosis of the tibial tuberosity just beneath the affected semilunar cartilage when comparison is made with the sound knee. These changes, however, are all indirect ones and there is a real need for direct visualization of the deformity of the semilurar cartilage. Sporadic attempts at endoscopy or the injection of opaque media, e.g., air or uroselectan, which have been carried out for many years have apparently not been of such consistent value as to justify the operative procedures involved and warrant more general use.

In 1932 Dittmar<sup>2</sup> published his observations in demonstrating the true articular space at the medial aspect of the knee in two patients by forcible abduction. He believed this was possible only in children or in adults where there was weakness of the collateral ligament. Felsenreich3 in 1935 reported observations on two patients showing subluxation of the medial meniscus, but said the procedure was rarely of value in demonstrating the semilunar cartilage, although it might be useful in testing the integrity of the collateral ligaments. A more complete study of the method was made by Nordheim4 in 1938. His observations in this paper were confined to normal individuals. He was able to show that forcible abduction or traction separates the articular cartilages, leaving a relative vacuum between them which provides contrast for the shadows of the cartilage. After a number of minutes of continued traction this vacuum is replaced by fluid withdrawr from the tissues. The converse of this ob-

<sup>\*</sup> Read at the Third Annual Clinical Conference of Mid-Western Radiologists, Detroit, Mich., Feb. 10-11, 1939.

servation is also true, i.e., the space can only be demonstrated when there is a negligible quantity of fluid within the joint. The joint space together with the internal semilunar cartilage was demonstrable in about 70 per cent of normal knees, while the external space was shown in only 2 of 30 attempts. Nordheim was also able to show

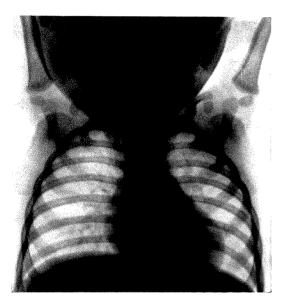


Fig. 1. A routine film of a child's chest showing the space between the articular cartilages at the shoulder joints produced by traction on the arms,

the true articular space by forcible traction at the phalangeal and shoulder joints.

For the past few months we have made observations with the method and believe that the results warrant consideration and further investigation. Occasionally the true articular space is visualized inadvertently as, for example, in children undergoing a chest examination with the arms raised and held close to the head (Fig. 1). Very often sufficient force is exerted to separate the cartilages at the shoulder joint and the space is revealed as a fine crescent shaped line. We have also seen the space at the hip joint when the child was forcibly restrained (Fig. 2). Rarely the true joint spacing is seen at the knee in the routine examination. Hippe and Hähle,5 in reviewing a large number of films, reported observing the space in 25 knees with arthronosos deformans, and in 5 apparently normal. Löhr and Hellpap<sup>6</sup>

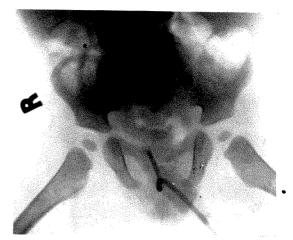


Fig. 2. The true articular space shown at the right hip joint in a child forcibly restrained.

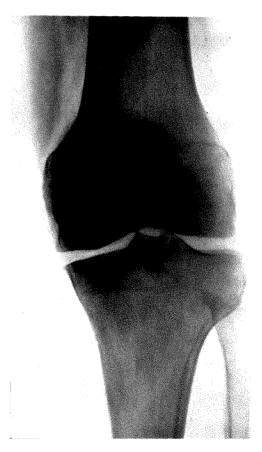


Fig. 3. The articular space at the medial aspect of the knee shown in a routine examination of a patient having osteo-arthritic changes and degeneration of the cartilage.

studied 642 films of the knee and observed the spacing only twice, once in a normal knee and in one with extensive degenerative changes. We have recently seen the space in a knee examined in the usual manner (Fig. 3). This patient was sixty-two years old and a retired police inspector who was working as a watchman. He had complained of weakness and pain in both knees for twelve years. Roentgen studies revealed well marked degenerative osteo-arthritic changes demonstrable on both sides. At the

and well padded at both ends is placed with one end against the external aspect of the knee joint and the other end against the chest of the examiner. Strong traction is then made by the examiner with the hands, on the thigh and lower leg. This is maintained for a period of five seconds to the limit of the examiner's strength or to the sensation of pain for the patient, when the exposure is made with the ray projected in





Figs. 4 and 5. The semilunar cartilage and the articular cartilages of the tibia and femur together with spacing between them shown by forced abduction in two normal knees.

medial aspect of the right knee was a dark linear shadow which we interpreted as the space between the articular cartilages. The mechanism of its production is not clear, but it has been observed to occur most often when there is degeneration of the cartilage, as in this case.

The technique which we have employed for the demonstration of the internal meniscus is very simple and requires no special apparatus. With the patient lying on his back and a small screen cassette under the knee, a cylindrical cone measuring about 25 cm. in length and a 8 cm. in diameter

a direction parallel to the upper surface of the tibia. This is best accomplished with very slight flexion at the knee. Only very rarely does the procedure cause the patient even temporary discomfort. We have found this method more fruitful than a mechanical screw device for exerting pressure. If the pressure is too long maintained Nordheim has shown that fluid is withdrawn from the tissues and the space is obliterated. The manual method permits a more careful regulation of the tension and also a small increment of tension may be applied at the instant of exposure.

The meniscus appears on the film as a long triangle with the base attached to the internal collateral ligament and the tip directed toward the tibial spines. The cartilaginous coverings of the tibia and femur are also shown. Our experience is in agreement with that of Nordheim who was able to show the cartilage in about 70 per cent of normal individuals. Figures 4 and 5 illustrate the findings in two normal young adults of each sex. Occasionally a mottled appearance at the joint is obtained (Fig. 6). This we believe is probably due to a droplet-like formation of the articular fluid as suggested by Nordheim. It is more difficult to show the external semilunar cartilage, but we were able to obtain a faint delineation of this structure in two children (Fig. 7). Fortunately it is not so important to

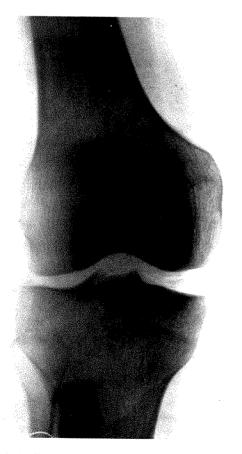


Fig. 6. A slight variation in the appearance of the spacing of a normal knee. The mottled appearance is probably due to the behavior of the articular fluid.



Fig. 7. Both internal and external articular spaces with the semilunar cartilages shown in a healthy child.

demonstrate this meniscus as it is much more rarely subject to injury than the internal semilunar cartilage.

An injury to the internal semilunar cartilage results in pain and effusion. For both of these reasons this method is not applicable to the study of the acute injury. It is also not to be used in old cases when there is evidence of effusion into the joint as there can be no expectation of demonstrating the space by separation of the cartilaginous surfaces. In such instances Schaer has recommended aspiration of a small amount of the fluid for bacteriological, cytological, and chemical studies and its replacement with 4-5 cc. of uroselectan and an anesthetic solution followed by roentgen studies in various projections. The results of such examinations, however, have not often been helpful and may be misleading. Nordheim favors the injection of air when fluid is present with the examination made in various positions so as to bring the air into contact with the structures in question.

The method which we have described is then suited only to cases of old injury where no effusion is present and here valuable information may be obtained. In Figure 8 are shown the findings obtained in A.S. who sustained an injury to his left knee ten years previously when broad jumping and who has had recurrent difficulties since.



Fig. 8. The articular spacing in both knees of a subject who suffered an injury to his left knee ten years ago.

A, the right knee presents a normal appearance while on the left, B, there is irregularity of the internal semilunar cartilage which represents the end-result of an old tear.

On the right side the semilunar cartilage presents a normal appearance while on the left there is a marked irregularity in the contour of this structure which we interpret as the result of an old tear.

It is not to be expected that this procedure will always or even usually yield conclusive results. In both the normal and abnormal case the semilunar cartilage may not be demonstrable. When it is demonstrated only gross abnormalities may be evident. According to Schaer important traumatic lesions may be present in the semilunar cartilage and warrant excision of the cartilage which are not evident to inspection at operation and which are revealed only by microscopic examination. Such lesions, of course, would not be revealed by this procedure. The procedure does give evidence of the integrity of the collateral ligaments which are of prime importance in the stability of the knee. On the affected side when there is weakness of the collateral ligament, forcible abduction will yield a greater space between the femur and tibia than on the normal side, as pointed out by Felsenreich. If, then, the uses and limitations of the method are understood, we believe this is an additional diagnostic procedure which will occasionally yield helpful information in the study of the knee joint.

#### REFERENCES

- Schaer, Hans. Der Meniskusschaden als klinisches, anatomisch-pathologisches und unfallmedizinisches Problem. Georg Thieme, Leipzig, 1938.
- 2. DITTMAR, O. Der Kniegelenk-Meniskus im Röntgenbilde. Röntgenpraxis, 1932, 4, 442-445.
- 3. Felsenreich, F. Darstellung des verletzten Meniscus medialis im Röntgenbild bei veralteter Kreuzband- und Seitenbandverletzung. Röntgenpraxis, 1935, 7, 331–333.
- 4. NORDHEIM, Y. Eine neue Methode, den Gelenkknorpel, besonders die Kniegelenkmenisken, röntgenologisch darzustellen. IV. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1938, 57, 479–495.
- 5. HIPPE and HÄHLE. Quoted by Löhr and Hellpap, ref. 6.
- 6. LÖHR, R., and HELLPAP, W. Der Kniegelenkspalt im Röntgenbild. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1938, 58, 45–56.

# OSTEOCHONDRITIS DISSECANS

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OSTEOCHONDRITIS dissecans, first described as a distinct pathologic entity and named by König in 1879, is a disease characterized by the separation, partial or complete, of a piece of articular cartilage, with or without part of the subjacent bone, from the ends of certain long hones

Munro in 1758 was the first to recognize that loose bodies in joints originated from the articular surface.

Paget thought that these joint bodies were caused by "quiet necrosis."

König in 1879 and in a subsequent paper in 1887 was really the first to classify osteochondritis dissecans as a definite entity. His description was that "without any injury fragments separate from articular surfaces. The bony surfaces of the fragments become covered with dense connective tissue and cartilage. A similar change takes place within the defect from where the fragment originated. At the same time, there is slight effusion and villous hypertrophy."

#### INCIDENCE

This is not a rare condition and has often been reported. It is most common during adolescence and early adult life and occurs more frequently in males.

It has been described in a number of joints including the hip, ankle and metatarsal articulations, but the far greater number appear to occur in the knee or elbow. While there is a tendency toward the inclusion of osteochondritis dissecans in one group having presumably the same etiology, namely, Köhler's, Legg-Perthes', Freiberg's, Kienböck's, Osgood-Schlatter's, etc., there are some who believe this disease a distinctly separate entity with a specific etiology. The reasons advanced for this belief are: (1) the characteristic roentgenological and pathological appearance; (2)

the circumstance that these changes occur not only almost exclusively in the knee or elbow, but in characteristic locations within these joints. In the knee, it is the lateral part of the internal condyle of the femur; in the elbow, the capitellum of the humerus.

#### ETIOLOGY

Several theories as to the etiology of the disease have been advanced which merit brief discussion. König, believing that the disease represented an inflammatory process, ascribed it to a low grade infection of unknown origin. Axhausen has suggested that the cause may be in small emboli of end arteries, resulting in infarction and a quiet, aseptic necrosis of the bone and cartilage deprived of its blood supply. Bernstein felt that the tendency to occur in families, and bilaterally in the individuals, suggests a constitutional abnormality, analogous to rickets, fragilitas ossium, coxa vara, etc. Phemister believes that the etiology may be similar to that of ununited fractures.

All investigators believe that trauma is predisposing. The trauma may represent direct violence, ligamentous pull or injury to arterial supply by long continued mild insults, as suggested by Sommer. Freiberg has further developed this viewpoint by the observation that in the knee the disease in its usual location is associated with a long tubercle of the medial tibial spine and that this may traumatize the involved area of the femoral condyle when the knee is in flexion and external rotation. Sommer and Fairbank have found a definite history of trauma in more than half of their cases.

Two other theories, that of fat embolism occluding the end arteries, and that regarding the process as a low grade arthritis or localized osteo-arthritis, have no supporting evidence.

### PATHOLOGY

The pathology of the disease has been formulated largely from gross inspection of the knee at operation and from examination of the excised specimen; little is known of the picture in the remaining main body of the involved bone.

The disease process begins at the point of greatest contact in the knee joint—i.e., most frequently the medial aspect of the most prominent inferior surface of the me-'dial condyle opposite the anterior tibial spine. Here a conical or discoid fragment of bone separates gradually from the underlying epiphyseal bone. The separation is gradual and may take months or years. Both the cavity and the separated side of the loose body become covered with fibrocartilage. Early in the process, the separating fragment may be held in place by a bridge of articular cartilage or synovia; or there may be at times only a fissure or circle of discoloration apparent in the articular cartilage, marking the limits of the underlying diseased plaque.

There are three stages then in which the

loose body may be found:

(1) Retained in the original bone cavity. Under these circumstances, the articular surface is convex and covered by hyaline cartilage; the deep surface will be rough and covered by fibrocartilage.

(2) Loose in the joint. Here the bodies tend to become rounded and may grow by accretion of new bone. The hyaline layer is usually changed into fibrocartilage. The separated body may break up into a number of smaller fragments.

(3) Attached to synovial villi. Sometimes a free body may become attached to synovial villi and a pedicle forms, resulting in rapid proliferation and enlargement of bone

and cartilage.

Microscopically the findings in the excised specimen are reported either as chronic inflammation or aseptic necrosis. The majority, however, have been unable to demonstrate inflammatory changes. In general, the degree of necrosis present varies inversely with the degree of attachment

as classified above. The defect in the bone may remain as such, or may fill in gradually after complete separation has taken place.

#### CLINICAL FINDINGS

The history is usually of several years' duration. Complaints are of soreness, stiffness and occasionally swelling of the involved joint. Locking is common, especially in cases with a completely separated fragment, but at times in patients where separation is not complete. King has described 4 cases in which the onset was acute subsequent to a mild trauma and presenting painful, tender, swollen joints locked in 15–45° flexion. In all of these cases, two or three loose bodies in the joint were demonstrated, and there can be little doubt that the process antedated the trauma and was merely unmasked by it.

Objective signs are few: demonstration of one or more loose bodies in such cases as these are present; sometimes fluid; some limitation of motion and wasting of the quadriceps in chronic cases. Axhausen has described a sign where, with the knee flexed, pressure upon the lateral aspect of the medial femoral condyle (the usual site of involvement) elicits an acute local tenderness.

Finally, cases have been described which are completely asymptomatic, this usually occurring in patients in whom the contralateral knee was clinically involved, and the second knee roentgenographed as a control

## ROENTGEN FINDINGS

Since there is nothing characteristic in the clinical picture of the disease, the diagnosis has been made roentgenographically in the great majority of cases. The lesion is best seen in the anteroposterior roentgenogram and is apt to be overlooked entirely in the lateral view. It consists of a defect, usually shallow and sharply defined at the typical location described above, and usually circular in outline. The immediately adjacent bone shows a narrow zone of increased density; there may be atrophy of

the bones as a whole in chronic cases. This defect may contain a separated or hinged fragment of bone which most frequently is partially decalcified, or it may be entirely ·empty. Richards and Freiberg have described 2 cases in which only a line of separation was seen in the roentgenogram with no decalcification, and the surgical finding was merely a fragment of bone, completely separated but held in position by intact articular cartilage. At the other extreme come those cases, of which our Case I is an example, in which a definite defect in the subchondral bone is demonstrated roentgenographically, but in which, on operation, only a discoloration, loss of lustre and roughening of the cartilage is found. If the fragment of bone and cartilage is actually free in the joint space, it may be, although often is not, radiopaque, and only the defect corresponding to its earlier site will be seen. In those cases in which one or more joint mice are present and are not decalcified to the degree of becoming translucent to the roentgen ray, they tend to migrate to the regions of the joint where they will interfere least with motion, i.e., the subquadriceps bursa and the posterolateral pouches. King has stressed the necessity for differentiating free bodies in the latter location from the sesamoid bones commonly found in the gastrocnemius tendons of origin.

#### DIFFERENTIAL DIAGNOSIS

The diagnosis is rarely made by clinical means; usually the patient is sent to the roentgenologist as a suspected case of torn medial meniscus, tuberculosis of the knee, or loose body. The other causes of loose body are:

(1) Synovial osteochondromatosis. This is a degenerative process involving the synovial membrane with calcification and tendency to form multiple loose bodies; however, in this disease there is no defect apparent in the underlying bone.

(2) Traumatic loose body is readily distinguished by the history of a preceding severe trauma and the presence of the bony

defect in the most exposed parts of the bone, whereas the osteochondritic lesion is located where it is least susceptible to external violence.

Osteochrondritis dissecans is differentiated from tuberculosis of the knee by the following criteria:

- (1) Tuberculosis tends to have much severer symptoms.
- (2) The tuberculous joint has in the roentgenogram a generally obscured appearance, while this is not true of osteo-chondritis dissecans.
- (3) In tuberculosis, there is usually a much greater degree of atrophy.
- (4) The location of the process is different—in osteochondritis dissecans the areas of the articular surface which have the most contact are involved, while in tuberculosis there is typically early destruction of areas in which there is little or no contact.
- (5) Sequestration in tuberculosis shows a sequestrum of increased density which preserves its line of articular cortex, while the surrounding bone is relatively atrophic and the articular cortex indefinite or destroyed; in osteochrondritis dissecans, the articular cortex is intact except in the sequestrated area, and the latter is of a similar or lesser degree of density than the adjacent bone.

In torn medial meniscus, the history and lack of characteristic roentgenographic changes should eliminate osteochondritis dissecans.

Hemophilic joints may at times show multiple, punched-out areas, and usually there is more than one joint involved. The clinical course of acute febrile episodes following trauma, multiplicity of the lesions and evidence of the disease elsewhere should serve to differentiate it.

The defects of skeletal tophi in gout are uncommon in large joints, rarely centrally located and the age incidence is distinct.

## TREATMENT AND PROGNOSIS

The treatment of choice is surgical. Fairbank states that the roentgenological dem-

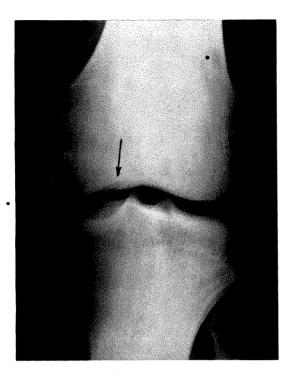


Fig. 1. Note concave appearance at the site of the lesion. No postoperative film could be obtained.

onstration of the lesion alone, unassociated with any symptomatology, does not constitute an indication for opening the joint. In the presence of symptoms, the majority of workers agree that radical extirpation of the detached or partially detached fragment, with or without curettage of the bony bed, is the ideal treatment. The results are almost uniformly good; for example. King in a series of 24 cases reports excellent results in two-thirds and unsatisfactory in only one-tenth. The course even without radical treatment is entirely benign; as our Case III will show, a satisfactory result may be achieved by immobilization alone in those cases in which the urgency of symptoms does not demand immediate surgical interference.

### CASE REPORTS

We would like to add 3 cases observed by us to the literature on the subject.

Case 1. A male, aged nineteen, occupation salesman, admitted on July 17, 1937, to the Montreal General Hospital with the history of

pain in the left knee for three to four years. The pain occurs on walking any considerable distance or when the knee has been kept in one position for more than a few minutes. It is localized to the joint line just medial to the patella and when most acute may be associated with swelling over the same area. There has been no limitation of motion nor genuine locking. There is no history of preceding trauma (?).

Examination shows slight swelling medial to the patella. A loose mass was felt over the joint line about I cm. medial to the patella. There was slight limitation of active extension.

Roentgen examination showed the typical punched-out defect of osteochondritis dissecans located at the lateral aspect of the medial condule of the femur (Fig. 1).

On July 19, the knee joint was exposed through an internal lateral incision. A small, rounded, elevated area the size of a ten-cent piece was seen on the articular cartilage of the medial condyle of the femur. This was removed completely with the scalpel, exposing raw bone underneath. The bed was not curetted. The medial semilunar cartilage was loose at its anterior attachment, hence it likewise was dissected free and removed. The pathologist reported degenerative non-inflammatory process in cartilage.

Postoperative course was uneventful and the patient was discharged on July 30. In the eight months since operation, he has had no symptoms

Whether the osteochondritis dissecans or the damaged meniscus was causing the symptoms here cannot of course be ascertained. Our second case, however, gives a history typical of torn medial meniscus; yet the latter was normal and the symptoms due entirely to osteochondritis dissecans.

Case II. A male, aged nineteen, whose chief complaint was locking of the left knee in flexion, accompanied by severe pain continuing for some hours after the locking itself had been released. This sequence of events had happened with increasing frequency for five years. Physical findings were limited flexion of the left knee with focal tenderness medial to the patella on the articular surface of the femur.

Roentgen examination on July 13, 1936, showed the characteristic annular defect in the articular surface of the medial femoral condyle (Fig. 2).

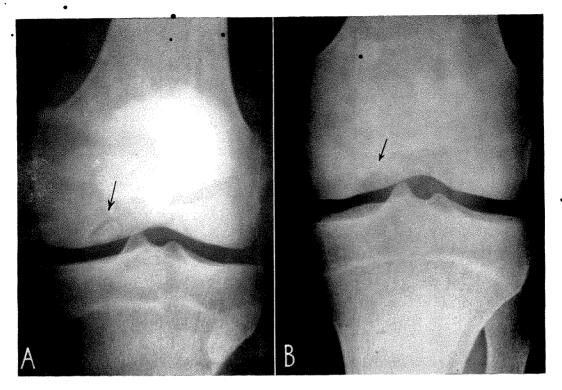


Fig. 2. Note prominent medial tibial spine.

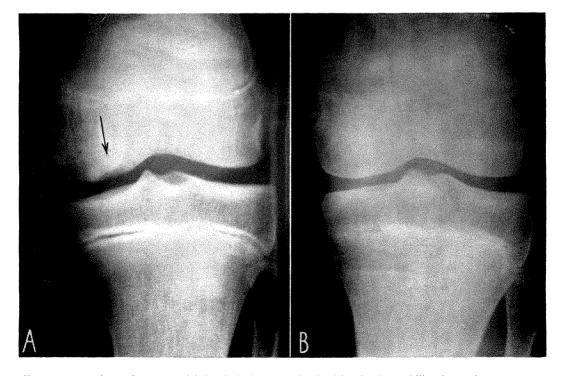


Fig. 3. A, no loose fragment visible; B, lesion completely filled in. Immobilization only treatment.

The knee joint was explored on July 14, 1936; necrosis of a dime-sized area on the posteromedial surface of the medial condyle was found involving the articular cartilage and extending into the subjacent bone. The necrotic cartilage and bone were removed; the bed was curetted smooth. The medial semilunar cartilage appeared entirely normal and was not removed. Histological examination of the specimen revealed chronic inflammation of cartilage.

One year and eight months subsequent to operation, the patient was asymptomatic. Reexamination showed almost complete filling in of the operative defect.

The 2 preceding cases were both treated radically, with satisfactory results. Our third case is presented to demonstrate that conservative treatment may be equally satisfactory in some instances.

Case III. A girl, aged twelve, who, with no history of injury, has complained of weakness and a sensation of "giving way" in the left knee. She has never actually fallen but states that the knee jerks forward and feels as though the bones were being twisted.

Examination revealed a healthy, robust child, walking without any limp or deformity. There is no swelling of the left knee by measurement; however, the lateral pouches appear fuller than those of the right knee. Motion, active and passive, is normal. There is half an inch atrophy of the left thigh. The knee shows some tenderness on pressure over the joint line anteromedially.

Roentgen examination of the left knee on May 23, 1936, showed a punched-out defect of the internal part of the medial condyle with a suggestion of condensation of bone in the articular surface of the tibia opposite.

Patient was placed in a cast subsequently.

Re-examination nine months later showed the punched-out area smoother and smaller. Symptoms have entirely disappeared. There was no limitation of motion or pain and no atrophy of the quadriceps.

#### SUMMARY

- (1) The literature pertaining to the etiology, pathology, clinical picture, roentgenological findings, diagnosis and treatment of osteochondritis dissecans has been briefly summarized.
- (2) Three typical cases of osteochondritis dissecans of the knee, showing interesting features with regard to diagnosis and treatment, have been added to the literature.

We wish to acknowledge our thanks to Drs. Goldman and Breitman for referring these patients to us.

#### REFERENCES

- BALENSWEIG, I. Osteochondritis dissecans of the knee. J. Bone & Joint Surg., 1925, 7, 465-468.
- 2. Bernstein, M. A. Osteochondritis dissecans. J. Bone & Joint Surg., 1925, 7, 319-329.
- 3. FAIRBANK, H. A. T. Osteo-chondritis dissecans. *Brit. J. Surg.*, 1933, 21, 67–82.
- 4. Freiberg, A. H. Osteochondritis dissecans. J. Bone & Joint Surg., 1923, 5, 3-17.
- 5. GEYMAN, M. J. Östeochrondritis dissecans. *Radiology*, 1928, 11, 315–319.
- GHORMLEY, R. K. Pathologic changes in diseases of joints. Am. J. ROENTGENOL. & RAD. THERAPY, 1933, 29, 729-735.
- 7. King, D. Osteochondritis dissecans. J. Bone & Joint Surg., 1932, 14, 535-544.
- 8. MILLER, L. F. Osteochondritis dissecans of capitellum of humerus. *Radiology*, 1936, 27, 237-230
- RICHARDS, G. E. Osteochondritis dissecans. Am. J. ROENTGENOL. & RAD. THERAPY, 1928, 19, 278–284.
- 10. Sommer, R. Die osteochondritis dissecans (König). Beitr. z. klin. Chir., 1923, 129, 1-60.



## IRRADIATION OF THE LONG BONES FOR GYNECOLOGIC BLEEDING\*

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FUNCTIONAL uterine bleeding is of perennial interest because of its frequency in gynecologic practice. A perusal of hospital charts reveals various diagnoses such as "ovarian insufficiency," "endocrine imbalance," "glandular cystic hyperplasia," "idiopathic or functional menorrhagia," etc., for unexplainable abnormal uterine bleeding. Many well-defined groups have been classified which respond to specific treatment. There is, however, one group of patients exhibiting this symptom which have defied the usual methods of treatment and have defied diagnosis as to its etiology.

All who have treated this condition have found a certain proportion of cases in which all orthodox treatment has been used without result. By orthodox treatment we include the use of uterine styptics, endocrine k-mostatics such as antuitrin S, progestin, thyroid extract, and curettage with or without intra-uterine radium.

A few years ago one of us, in calling for a complete blood count in a case of long continued intractable uterine bleeding, received a pathological report which included the blood platelet count. With the exception of a slight secondary anemia, the platelet count was the only abnormal finding. This seemed to be significant in view of the fact that there were no abnormal anatomical findings and that every known method of treatment listed above had been used unsuccessfully. Because of its efficacy in idiopathic thrombocytopenia purpura, irradiation of the spleen was instituted with immediate startling results. Not only did the uterine bleeding cease abruptly after a continuance of at least two years, but the blood platelet count returned to normal and subjectively the patient experienced a new sense of well-being. Therefore,

in all cases of functional bleeding we have had blood platelet examination in order to segregate this intractable group of cases.

We have been unable to find in the literature any attention being given to the dyscrasia of the blood platelets in relation to this condition. In the Year Book of Obstetrics and Gynecology for 1937 we have found the following abstract entitled, "Irradiation of spleen for gynecologic bleeding."

At the Berlin Woman's Clinic, P. Caffier observed twelve girls with juvenile hemorrhages during 1926 to 1934 who were treated by means of x-rays applied to the spleen. In five cases there was complete success, and in four cases temporary relief. In four of the five permanently successful cases not only did bleeding cease after two to three days but the menstrual periods became regular. This treatment is harmless and may be used at any age. It probably acts by producing a breakdown of thrombocytes. The author believes that this form of therapy should be combined with modern hormone therapy directed at the cause of bleeding.

Caffier also suggests irradiation of the spleen for bleeding which is due to uterine myomas, especially when roentgen ray treatment locally applied to the fibroids does not bring about a sufficiently rapid cessation of bleeding. The action of irradiation of the spleen is rapid. The author has seen bleeding stop six hours after treatment, hence he believes that this treatment should be used whenever prompt cessation of uterine bleeding is imperative.

It is noteworthy that in this abstract no mention is made of the blood platelet count as a diagnostic or therapeutic aid.

Baer states,

Thrombocytopenic purpura, one of the rare diseases, may present in addition to the usual extravasations, bleeding from the uterus. The diagnosis is based on the decreased platelet count, increased bleeding time and clinical

<sup>\*</sup> Read at the Twenty-fourth Annual Meeting, American Radium Society, St. Louis, Mo., May 15-16, 1939.

manifestations. The best available treatment is repeated blood transfusions. In the more severe instances of the disease splenectomy has been performed.

We know that splenectomy, although usually associated with remarkable improvement in cases of thrombocytopenic purpura, may also be of no benefit. In those cases when the spleen is overactive and destroys the platelets its removal is indicated. We think that in these cases the disturbance in the production of the platelets is in the bone marrow and splenectomy is of no value.

Wright has shown that the megakaryocytes perform the extremely important function of giving rise to the blood platelets. The blood platelets commonly vary between 200,000 and 600,000 per cubic millimeter. The age of the individual causes the red cells and platelet count to vary toward the high normal level in infancy and childhood and to swing toward the low level after the fiftieth year.

Minot pointed out that in certain purpuras any agent bringing about red cell destruction operates against the platelets and megakaryocytes. The platelets ordinarily vary in number in proportion to the vigor of the red cell formation, and at the moment of examination they may be greatly reduced independently of the red cell change. The cause of this destructive process has not been determined. The fact that Lee and Robertson by repeated injections of guinea pig platelets into rabbits have succeeded in producing serum which would destroy the platelets of the guinea pig with consequent purpura is of interest in this relation.

Because there were no other symptoms of purpura in cases under consideration it seemed reasonable that the diminution in the number of platelets was due to a deficient formation in the bone marrow rather than in an increased destruction by the reticulo-endothelial system (primarily the spleen). Therefore, irradiation of the long bones was instituted rather than the irradiation of the spleen. There being no general

symptoms of purpura to indicate a diagnosis we have designated this condition as uterine purpura.

We report herewith a few typical cases:

CASE I. M. M., aged twenty-one, single.

Family history negative. Past history: tonsillectomy 1929, appendectomy 1934. Menses began at the age of fifteen, irregular and always late and scanty. Present illness began two years ago with uterine bleeding. Has had four curettements and two applications of radium, at each time was given 1,500 mg-hr. filtered through I mm. of platinum. Patient did not know exact dates. This only improved her condition temporarily. Physical examination on May 8, 1936, showed no demonstrable abnormalities. Blood examination was essentially negative except that the platelet count was 91,000.

Date	Platelet Count	Treatment						
5-8-36	91,000							
5-9-36		100 r to each femur						
5-10-36	I 20,000	100 r to each tibia and fibula						
5-11-36	160,000	100 r to each femur						
5-12-36	240,000	100 r to each tibia and fibula						
5-13-36	290,000							

Menses were normal for six month. Following the menses on November 2, 1936, she continued to bleed. Platelet count on November 16, 1936 was 86,000.

Menses returned to normal and were of the twenty-eight day type and of five day duration. They remained normal until patient moved away in October, 1938.

Case II. M. S., aged twenty-one, single.

Patient has had continuous uterine bleeding for two years. Past history and family history negative, no surgery except tonsillectomy. Menses began at the age of thirteen, always irregular and tended to be scanty rather than profuse. Two years ago continuous uterine bleeding began. All usual treatments were used without results, including two curettements. During this time patient has had a sense of ill-being, with a feeling of lassitude and was easily fatigued. Physical examination negative.

Blood examination November 23, 1937, reported by Dr. Kretschmer was as follows:

Red blood count 4,240,000; hemoglobin 96 per cent; white blood count 11,300; platelet count 28,000.

. Date	Platelet Count	Treatment
II-23-37	28,000	
11-24-37		100 r to spleen
II-27-37	101,000	100 r to spleen
11-29-37	82,000	
I2- I-37	78,000	
12- 2-37		100 r to each tibia and fibula
12- 3-37	124,000	
12- 4-37		100 r to each femur
12-7-37	270,000	
12- 9-37	Menses n	low normal
12-30-37	65,000	100 r to each tibia and fibula
I- 3-38		100 r to each femur
I- 5-38	144,000	
I- 6-38		100 r to each tibia and fibula
1-11-38	155,000	
1-13-38		100 r to each femur
1-19-38	178,600	
1-30-38	Married.	Last report menses normal
9-29-38	182,000	Has not menstruated since
		5-28-38. Pregnant
11-23-38	112,000	
2- 1-39	199,000	

The coagulation time on November 23, 1938, was 4 min. 30 sec., and on February 1, 1939, was 4 min. 35 sec.

Patient had no treatments after January 13, 1938, and had no disturbance of menses. She was married on January 30, 1938, became pregnant in May and during the pregnancy the platelet count dropped as shown above. She was delivered March 5, 1939, of a normal healthy child. Patient refused to have any more blood counts.

#### Case III. Mrs. A. I., aged twenty-six.

No serious illnesses. Menses began at the age of twelve and were regular until the age of fifteen. They were of the twenty-eight day type, four days' duration. At fifteen began to menstruate every two weeks. At the age of sixteen began to spot some every day, continuing for two years. She was sent to a lower altitude but continued to be irregular. Ergot was given but this did not change the menses. She was curetted at the age of nineteen, following which menses were regular for six months, then the irregularity returned. Anterior pituitary-like hormone and other hormones were given with no change in the spotting. In 1935, she was curetted again and a cystic tumor was removed from the ovary. Menses were regular for six months and then symptoms recurred. It was then reported that the curettage findings showed a hyperplasia. Physical examination showed no demonstrable abnormalities. On August 23, 1938, patient was given 300 r anteriorly over the uterus and ovaries. August 26, 1938, patient was given 300 r posteriorly over the uterus and ovaries.

Patient had normal menses on September 5 and had no spotting. She reported October 15 that she had had no menses or spotting. October 25 patient began to have pain in the lower right abdomen.

The Aschheim-Zondek test was negative. October 31 exploratory laparotomy revealed tubal pregnancy. The right tube and ovary were removed. Menses in November were normal. Menses in December were of fourteen days' duration. Menses in January were irregular and patient continued to spot. She was given snake venom solution with no improvement. She was again referred for therapy. The blood examination on February 4, 1939, reported by Dr. Kretschmer was as follows: Red blood count, 4,890,000; hemoglobin, 92 per cent; white blood count, 7,200; small lymphocytes, 24 per cent; large lymphocytes, 12 per cent; neutrophiles, 61 per cent; eosinophiles, I per cent; monocytes, 2 per cent. There was a very slight poikilocytosis and a slight anisocytosis. The platelet count was 189,320. Coagulation time was 6 minutes and 40 seconds.

Date	Platelet Count	Treatment	Coagulation Time
2- 4-39	189,320	100 r to each fe- mur	6 min. 40 sec.
2- 8-39		100 r to each tibia and fibula	
2-13-39		100 r to each fe- mur	
2-14-39	Spotting	ceased	
2-17-39		100 r to each tibia and fibula	
2-20-39		100 r to each fe- mur	
2-24-39	134,000	100 r to each tibia and fibula	5 min. 20 sec.
2-27-39	Normal n	nenses	
3- 8-39		100 r to each fe- mur	
3-29-39	148,000		6 min. 30 sec.
3-29-39	No spotti	ing or menses since	2-27-39
4-28-39	No spotti	ing or menses since	2-27-39

This case did not show any marked change in platelets but nevertheless her abnormal bleeding ceased. Patient has gained 5 pounds and is still under observation.

#### CASE IV. P. S., aged thirteen. •

Patient had no operation or serious illness. Menses began at the age of eleven and were of five days' duration. Menses were regular until two months ago when they changed to every two weeks and four day duration. No other symptoms. Physical examination negative. Blood examination on May 11, 1938, reported by Dr. Kretschmer was as follows:

Red blood count, 4,820,000; hemoglobin, 90
•per cent; white cell count, 13,600; neutrophiles,
71 per cent; small lymphocytes, 17 per cent;
large lymphocytes, 4 per cent; eosinophiles,
2 per cent. Coagulation time 7 minutes and 30
seconds. Platelet count was 197,000. On June
13, 1938, platelet count was 110,000.

Date	Platelet Count	Treatment	Coagulation Time
6-13-38		100 r to each fe- mur	4 min. 50 sec.
6-15-38	193,000	100 r to each tibia and fibula	
6-21-38	154,500	100 r to each fe- mur	
6-28-38	173,000	100 r to each tibia and fibula	3 min. 15 sec.
7- 2-38	149,000		3 min. 30 sec.
7- 8-38	270,000		4 min. 15 sec.
7-10-38	Normal m	ienses	
7-20-38	280,000		3 min.
8-15-38	213,200		4 min. 10 sec.
8-29-38	253,000	100 r to each fe-	2 min. 30 sec.
		mur	
9- 6-38	199,000		3 min.

The menses became regular and have continued to be regular twenty-eight day type and of five days' duration. Patient has no symptoms.

We have treated several cases empirically with snake venom solution (cobra H.W.D.) using I cc. hypodermically three times weekly. The following is a typical case.

#### CASE v. R. B., aged nineteen.

Family history: mother died in patient's early childhood, no knowledge of her menses. There are three sisters of whom one had some type of menstrual disturbance which soon became normal. Past history: for other illnesses essentially negative. Menses began at the age of fourteen, were irregular for three years,

regular for one year, and again irregular until October, 1938, when uterine bleeding became constant although variable in amount. Physical examination showed no demonstrable abnormalities.

Date	Platelet Count	Coagulation Time
12-12-38	121,000	5 min.
12-19-38	191,000	6 min.
12-27-38	199,500	4 min. 15 sec.
1- 3-39	158,000	4 min. 45 sec.
1-10-39	198,000	4 min. 30 sec.
1-17-39	165,000	10 min.
1-24-39	153,000	6 min. 20 sec.
2- 1-39	181,000	5 min. 50 sec.

Menses last of December and January were normal. Menses in February became continuous and irradiation was begun over the long bones.

Date	Platelet Count	Treatment	Coagulation Time
3-6-39	106,000		5 min. 15 sec.
3- 7-39		100 r to each fe- mur	
3-11-39		100 r to each tibia and fibula	
3-14-39		100 r to each fe- mur	
3-18-39		100 r to each tibia and fibula	
3-21-39	125,000	100 r to each fe- mur	3 min. 45 sec.
4-18-39	156,000		3 min. 30 sec.

Menses returned to normal twenty-eight day type and of five days' duration.

#### Technique Used.

Case 1: 200 kv., 50 cm. distance; filtration 0.5 mm. copper and 1 mm. aluminum. Field,  $4 \times 10$  inches, focusing over the middle of each femur and each tibia.

Case II: Same as Case I except filtration was 0.75 mm. copper and I mm. aluminum.

Cases III, IV and V: 200 kv., 50 cm. distance, filtration 1.75 mm. copper and I mm. aluminum. Field, 10×20 cm., focusing the same as in Case I.

While studying Case I (a student nurse), we had platelet counts made on a group of normally menstruating nurses. These girls were chosen because of no stigmata of endocrine dyscrasias. Of these, 10 showed above 200,000 platelets and 2 showed below 200,000 but above 150,000 platelets. It

is our impression that uterine bleeding does not occur in the early months of platelet anemia. We feel that it is the long continued deficiency which tends toward the production of bleeding. We must also consider that platelet anemia may be an effect of long continued bleeding with a fatigue of some elements of the hemopoietic tissue and that treatment as described restimulates the production of the platelet precursors. We have not been able to determine any critical platelet level at which bleeding constantly appears. In this connection we must not lose sight of the effect of the individual's endocrines in affecting the situation. It may be that individuals with high blood estrin concentrations would have bleeding with only a small platelet deficiency while those with low estrin concentrations or estrin concentrations balanced by progestin would have bleeding only at lower platelet levels. The same may also be true in thyroid variation. It may be significant that 90 per cent of the cases we have studied were under twenty-five years of age.

The effect of platelet anemia on the maintenance of pregnancy has not been investigated adequately because of a lack of material. One of the cases reported in detail above experienced a normal pregnancy even though the platelet count decreased to 112,000 returning spontaneously before delivery to 199,000.

Another case treated for this type of bleeding with successful recovery showed a marked decrease in platelet count in the third month of pregnancy. She miscarried in the fifth month in the Denver General Hospital and no record of the platelet count was obtainable.

Still another case showing intermittent spotting beginning at her second month of pregnancy was treated with progestin and vitamin E. She began more active bleeding in the fifth month. The platelet count then was 50,000. She was treated with snake venom solution 0.5 cc. three times daily with a consistent rise in platelet count to 260,000 in five days. She miscarried, however,

on the same day her platelet count reached normal. The placenta showed evidence of separation during this five day period. One month following the miscarriage she began what she considered a menstrual period which was excessive. Her platelet count at that time was 58,000. She is under radiation treatment at the present time.

We have had no experience in these cases with the use of vitamin K or the antimenorrhagic factor from liver recently introduced. It would be interesting if those who are experimenting with these substances in the treatment of uterine bleeding would check platelet counts and determine whether therapeutic effect and increased platelets are coincidental. We realize that error is great in determining platelets. Dr. O. S. Kretschmer who examined the blood in our series has developed a method by which in multiple counts they correspond within 10 per cent.

#### CONCLUSIONS

- 1. We have described a group of cases of functional uterine bleeding which have been intractable to all ordinary forms of treatment. These cases have shown a decrease in the platelet count as the only positive abnormal finding.
- 2. Treatment of the long bones by small doses of radiation has in almost all instances relieved the bleeding.
- 3. The cessation of symptoms has been coincidental with a return of the normal platelet count.
- 4. We have used snake venom solution with similar immediate results but with less prolonged effect.
- 5. Since there are no other abnormal general findings or other specific symptoms of purpura, we have designated the condition as uterine purpura.

#### REFERENCES

- BAER, J. L. Benign uterine bleeding. Surg. Clin. North America, 1939, 19, 149-160.
- CAFFIER, P. Zur Frage der Milzbestrahlung bei gynäkologischen Blutungen. Zentralbl. f. Gynäk., 1937, 61, 1874–1876.

3. Lee, R. I., and Robertson, O. H. Effect of antiplatelet serum on blood platelets and the experimental production of purpura hemorrhagica. J. Med. Research, 1916, 33, 323-336.

4. Minot, G. R. Diminished blood platelets and marrow insufficiency; a classification and differential diagnosis of purpura hemorrhagica, aplastic anemia and allied conditions. *Arch. Int. Med.*, 1917, 19, 1062–1084.

5. Wright, J. H. The histogenesis of blood platelets. 7. Morphol., 1910, 21, 263-278.

#### DISCUSSION

• Dr. Abraham Strauss, Cleveland, Ohio. I would like to ask if any of these patients had large spleens and what the indication was for irradiation rather than splenectomy.

DR. WILLIAM P. HEALY, New York City. I would like just to comment on one point, and that is that these women are all apparently very young, and any form of therapy that will permit us to keep radiation out of the pelvis and yet control the disease is worth while, because we know that intra-uterine irradiation is to be avoided on account of its deleterious effect upon ovarian activity.

It was interesting to me, however, to note that in one of the cases that was reported in this series to have conceived and gone to term, the patient before coming under Dr. Bouslog's and Dr. Evans' observation was said to have been treated twice with intracavitary irradiation amounting to 1,500 milligram-hours each time without controlling the uterine bleeding, and subsequently conceived and went to term and was delivered of a normal baby.

Of course that is an item that should be received a little skeptically (as to the amount of irradiation, etc.), at least from our angle.

I still would like to say that keeping irradiation out of the pelvic field in these young women is important.

I am extremely interested in the essayists' paper and in their results and findings. Irradiation of the spleen has been the form of treatment that we have usually carried out in these cases with a fair degree of success. In only one case have I used snake venom and that patient had a general purpuric reaction, of the other mucous membranes as well as the uterine, and she also had curettage and small transfusions.

She responded at once and satisfactorily to the snake venom serum. Bleeding terminated and menses became normal.

Dr. Evans (closing). This has been an interesting series of cases to Dr. Bouslog and myself in that we were unable to find anything in the literature concerning this particular group of cases.

In answer to the question about the spleen, there were no enlargements of the spleen in any of the cases that we saw, and the cases were not serious enough to consider splenectomy.

One point I want to stress is that there is apparently no critical level of platelet count. That, as we tried to bring out in the paper, is probably due to hormonal variation of the individual.

In comparing this treatment to the treatment with snake venom, the snake venom apparently brings up the platelet level very rapidly and the uterine bleeding usually ceases, but within a few weeks of the cessation of the snake venom treatment, the platelets drop down to their low level again and bleeding recurs.

It has been our impression that, while in every case the first group of radiation treatments has not completely relieved the individual, the relief has been of longer duration and that subsequent irradiation has given apparent cure over a much longer period of time.

The value of this, as Dr. Healy has said, is because we find it in young women and we do not have to destroy the reproductive function.

Another group of cases that is interesting to me is the group of women who miscarry for no reason: Those whom we have always told that they had an imperfect implantation or an infantile uterus or some such excuse in order to allay their apprehension. We haven't had enough cases yet to know whether this is a factor in miscarriage or not.

It is very likely, however, that there is a certain group of women who miscarry, in which the cause is due to this platelet count. From now on I am going to have platelet counts taken on all women who present themselves as obstetrical cases.





## POST-IRR ADIATION CHANGES IN THE LUNGS AND THORAX

# A CLINICAL, ROENTGENOLOGICAL AND PATHOLOGICAL STUDY, WITH EMPHASIS ON THE LATE AND TERMINAL STAGES\*

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RADIATION damage to the lungs and pleura has been observed and reported by numerous radiologists since Groover, Christie and Merritt directed attention to this complication. Prior to this study, only a few unsubstantiated reports were published of such injury. These clinical observations have been corroborated by careful animal experimentation by many investigators. An exhaustive search of the literature has not revealed any records of patients, so injured, who were followed for many years.

has been selected because of special features we wish to present. Of the 18 cases, 11 died and postmortem studies were done on 8.

The case histories of all the patients follow. Included are the details of dosage, the relevant clinical features and roentgen studies, and finally, the postmortem findings where this examination was made.

#### CASE REPORTS

Case I. A. B., female, aged forty-six\* (Table I).

TABLE I

Year	Month	Field	Dose	Kv.	Ma.	Filter	Dist.
1934-	12/8-	L. ant. axilla and supraclavicular L. post. axilla and supraclavicular	1600 r† each	200	8	o.5 mm. Cu	50 cm
1935	1/20	L. axilla directly	300 r	200		ı mm. Al	50 cm
		L. ant. chest wall 20 ×20 cm. L. ant. chest wall 20 ×20 cm.	1000 r	200 I40	8	plus	50 cm

It is the purpose of this paper to describe the roentgen, clinical and pathological findings of all the stages of radiation damage to the lungs. Outstanding among the late manifestations in several cases is the terminal picture of severe pulmonary fibrosis associated with signs of right heart failure. The latter has not, as yet, been described in the literature on radiation pneumonitis.

#### MATERIAL

The material to be presented consists of 18 cases, which were followed for periods up to twelve years following treatment. This series does not represent all the cases of pneumonitis observed in our clinic but

Status on Admission, December 8, 1934. Postoperative carcinoma of the left breast referred for prophylactic irradiation.

Treatment. One course of moderately intensive irradiation. Average dose, high voltage 250 r, medium voltage 175 r.

Course. Sticking pain appeared in the left chest five weeks following irradiation. Roent-genograms of the lungs now showed linear infiltrations in the left hilum. During the next two months, films showed increase in the left hilar infiltrations, tenting of the left diaphragm and adhesions between the pleura, diaphragm and heart on the left. Fever, sweating and severe precordial pain appeared six months after

<sup>\*</sup> Case taken from Dr. Freid's private practice.

<sup>†</sup> For all case reports r measurements are in air unless otherwise indicated.

<sup>\*</sup> Read in part before the New York I regen Ray Society, New York City, March 20, 1939.

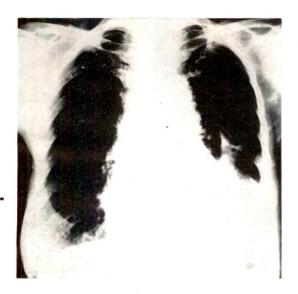


Fig. 1. Case 1. Pleural, pericardial and interlobar effusions six months following irradiation.

irradiation. Dry cough and dyspnea followed soon thereafter. Films now showed partial resolution of the hilar infiltrations, less tenting of the left diaphragm, slight left interlobar pleurisy and pericardial effusion. Sticking pain appeared in the left medial chest nine months after irradiation. From this point on, symptoms and roentgenograms of the chest showed progressive improvement. Two years later, the patient had no complaints, and roentgenograms of the heart and lungs were practically normal. The skin now showed moderate telangiectasia.

CASE II (Monte, Hosp. Rad. Cl. No. 3675). P. B., male, aged forty-three (Table II).

Status on Admission, October 7, 1937. Carcinoma of the left upper lobe bronchus.

Treatment. Intensive irradiation given, cross-firing lesion from several fields. Two fields daily, each receiving 250–300 r, treated November 19, 1937; thereafter only single fields.

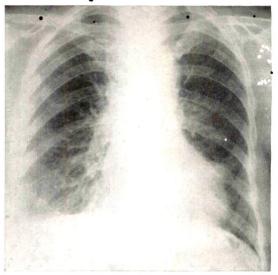


Fig. 2. Case I. Few hilar infiltrations persist. Percardial, pleural and interlobar effusions completely absorbed.

Course. Initial cough and pain disappeared immediately following irradiation. One month later, the patient developed cough, dyspnea and fever. The original lesion, on coentgen examination, had been noted on the left side, between the 3rd and 4th ribs. By November 1, 1937, it had receded under therapy. The follow-up film of January 22, 1938, showed a number of soft irregular infiltrations in the treated lung field, also some clear honeycombed areas, the largest suggesting a cavity. With the recurrence of cough on January 30, 1938, patient developed pneumonic signs in the involved area and severe dyspnea. He died of a pulmonary hemorrhage, six weeks after irradiation.

Postmortem Examination.\* The left lung was homogeneously gray; below the upper lobe bronchus was a large cavity containing foul

\* We are indebted to Dr. Fulstow, pathologist to the Norwalk Connecticut General Hospital, for the postmortem findings.

TABLE II

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1937	10/7-10/29	L. ant. chest, upper L. post. chest, upper	15 ×15 cm. 15 ×15 cm.	3400 r 3100 r	200	25	1 mm. Cu plus 4 mm. Al	80 cm.
1937	11/4-12/23	L. ant. chest, upper and inner L. ant. chest, upper and outer L. post. chest, upper and inner L. post. chest, upper and outer L. ant. lat. chest L. post. lat. chest	10 ×8 cm. 10 ×8 cm. 10 ×8 cm. 10 ×8 cm. 10 ×10 cm. 10 ×8 cm.	900 r 900 r 1200 r 1200 r 1200 r 3000 r 2700 r	200	25	1 mm. Cu plus 4 mm. Al	80 cm.

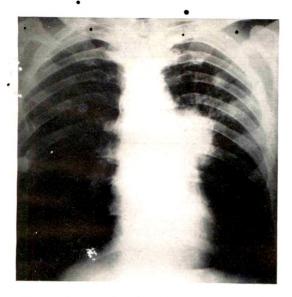


Fig. 3. Case II. Mass in the left lung extending out from the left hilum.

pus; the bronchi were filled with blood clots. Microscopic study revealed bronchopneumonia with purulent bronchitis, and numerous foci of necrosis. Fibrosis masked the picture, so that no definite carcinoma could be seen.

Case III (Monte. Hosp. Rad. Cl. No. 2305). H. B., female, aged thirty (Table III).

Status on Admission, April 28, 1933. Lymphosarcoma involving the left tonsil, left cervical nodes and right mediastinum.

Treatment. Daily dose 250 and 330 r first course; 250 r other courses.

Course. Roentgenograms ten days following Course I showed a few infiltrations in the right upper medial lung. About five weeks later, patient developed pain in the right posterior chest and a productive morning cough. Roentgenograms now showed many fluffy infiltrations in the upper right lung. Symptoms and infiltra-

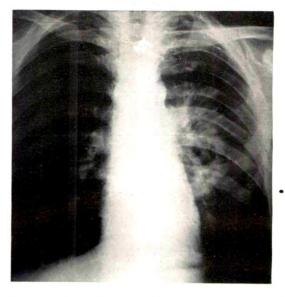


Fig. 4. Case II. Following irradiation. Number of soft irregular infiltrations in the medial half of the left lung. Few areas of rarefaction in this region suggesting cavitation.

tions disappeared over a period of three months. The patient then developed left supraclavicular nodes and slight widening of the left superior mediastinum. Following Course II, cough reappeared, also general malaise. Two months following Course III, roentgenograms showed further widening of the left superior mediastinum, infiltrations in the adjacent left lung and tenting of the left diaphragm. The patient now developed bilateral bronchopneumonia and died two weeks later.

Case IV (Montefiore Hospital No. 18123). F. G., female, aged nineteen (Table IV).

Status on Admission May 10, 1929. Hodg-kin's disease involving supraclavicular and mediastinal nodes.

TABLE III

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1933	4/28- 5/21	R. and L. ant. mediastinum Post. mediastinum	15 ×8 cm. 15 ×12 cm.	1880 r each 1640	200	30	0.5 mm. Ag plus 1 mm. Al	50 cm.
1933	10/10-	L. supraclavicular region	7×9 cm.	2000 r	200	4	o.5 mm. Cu plus 1 mm. Al	50 cm.
1933	11/14- 12/15	L. ant. mediastinum L. post mediastinum	10 ×15 cm. 10 ×21 cm.	1900 r 1480 r	200	4	0.5 mm. Cu plus 1 mm. Al	50-80 cm.

TABLE IV

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1929 I	5/14*- 6/28	L. ant. and post. chest R. ant. and post. chest	16 ×13 cm. 20 ×12 cm.	1800 r each 1725 r each	200	30	0.5 mm. Ag plus 1 mm. Al	50 cm.
1929 11	8/13- 9/4	L. ant. and post. chest R. ant. and post. chest	16 ×13 cm. 20 ×12 cm.	1650 r each 1650 r each	200	30	0.5 mm. Ag plus 1 mm. Al	50 cm.
1929 111	9/25- 12/12	R. and L. post. chest	20 ×12 cm.	2500 r each	200	30	o.5 mm. Ag 1 mm. Al	50 cm.

Treatment. Individual doses varied from 250 to 330 r.

Course. Mediastinal nodes smaller and general condition improved after first course of ir-

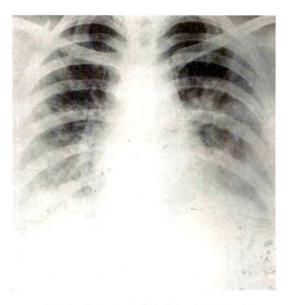


Fig. 5. Case iv. Soft infiltrations lower two-thirds of both lungs.

radiation. Dyspnea and slight cough present on admission persisted. Following second course of radiotherapy, patient gradually declined, although roentgenograms showed further recession of the mediastinal nodes. Dyspnea and cough were worse and pain appeared in the chest. Roentgenograms now showed soft infiltrations in the lower two-thirds of both lungs, slight elevation of the left diaphragm, a few pericardio-diaphragmatic adhesions and slight enlargement of the heart. The third course of irradiation was given because the pneumonitis was not recognized. One month later, patient developed tachycardia, palpitation and cyanosis. She died within a few weeks with symptoms of diffuse bronchopneumonia.

Postmortem Examination. The lungs showed at lectasis, patchy cellular fibrosis, areas of hyalinization and hemorrhage, also bronchiolar dilatation. The lymph nodes were diffusely fibrotic. A small effusion was present in the pericardium. The right auricle and ventricle were increased in size. The left heart was negative.

Case v (Montefiore Hospital No. 29005). E. B., female, aged forty-two (Table v).

Status on Admission, January 7, 1938. Unoperated carcinoma of right breast; post-irradiation. No evidence of local or distant disease at this time. Some pain present over the right upper chest.

*Treatment.* The irradiation was all given at another institution. The original mass in the breast had completely receded.

Course. Dry cough and right shoulder pain

TABLE V

Year	Month	Field	Dose	Kv.	Ma.	Filter	Dist.
1937	5/28-	R. breast, upper	2000 r	200	30	o.5 mm. Cu	50 cm.
	6/25	R. breast, lower	2000 r			plus	
		R. breast, lateral	2000 r			ı mm. Al	
		R. supraclavicular region	2000 r				
		R. axilla, direct	2000 r				
		The five fields were treated in rotation,					
		250 r per treatment					

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Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1934 1935	II/28- I/2	Ant. mediastinum Post. mediastinum	15×15 cm. 15×15 cm.	2100 r 2100 r	200	30	o.5 mm: Ag plus 1 mm. Al	50 cm.

were noted three months following radiotherapy, lasted seven to eight months, and then disappeared. A chest film, taken four months after irradiation, showed some fibrosis of the right upper lobe which had been clear before treatment. The fibrosis became sharper in appearance on later films. The skin showed induration and some telangiectasia. The patient later developed skeletal, pulmonary and cerebral metastases in the order named, and died in August, 1939.

Case VI (Montefiore Hospital No. 26217). P. C., female, aged fifty-five (Table VI).

Status on Admission November 23, 1934. Lymphoblastoma of the mediastinum with symptoms of mediastinal compression.

*Treatment*. One field daily. Dose 100 r at onset; later 150 r.

Course. Immediately following the irradiation, the lungs and mediastinum became negative. Roentgenograms ten weeks later showed exaggeration of hilar shadows, streaky infiltrations radiating out from the left hilum, and soft confluent infiltrations in the upper right lung. Cough and dyspnea persisted when mediastinal pressure was relieved, due to appearance of pneumonitis. Onset of pain in the right shoulder radiating down the arm, also right interscapu-

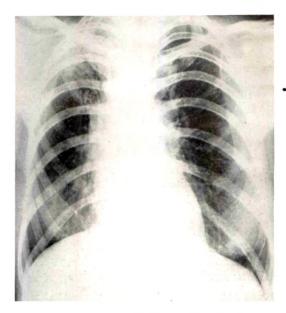


Fig. 6. Case v. Moderate fibrosis of right upper lobe.

lar pain. Roentgen signs increased for six weeks and then slow resolution set in. Roentgenograms three years later show only slight fibrosis in the hilar areas and upper lobes. Occasional non-productive cough and dyspnea have persisted to the present.

TABLE VII

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1933	4/17- 6/24	R. breast, axilla, supraclavicular	20 ×20 cm.	1400 r (ayerage dose 400 r)	200	5	o.5 mm. Cu plus 1 mm. Al	50 cm.
1934	2/2- 3/13	R. breast, axilla, supraclavicular	20 ×20 cm.	2000 r (average dose 500 r)	200	5	0.5 mm. Cu 1 mm. Al	50 cm.
1935	4/15	R. breast, ant., one exposure R. axilla, direct, one exposure R. axilla and supraclavicular, post., one expos.		750 r 750 r 750 r	200	5	o.5 mm. Cu plus 1 mm. Al	50 cm.
1935 1V	9/23- 9/26	Course III repeated			200	5	0.5 mm. Cu plus 1 mm. Al	50 cm.
1937 V	3/11-3/17	R. supraclavicular. Radium element pack		24000 mg-hr.		-		

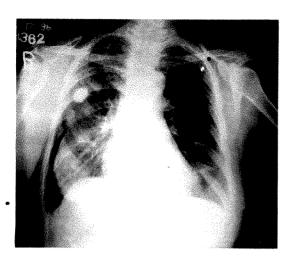


Fig. 7. Case viii. Diffuse haziness and fibrosis right upper lobe. Few calcific plaques in right anterior chest wall opposite 2nd and 3rd anterior ribs; 2nd 3rd, 4th and 5th right anterior ribs show old fractures with eburnation of the ununited ends resulting in a type of pseudarthrosis.

CASE VII (Montefiore Hospital No. 29119). C. R., female, aged fifty-five (Table VII).

Status on Admission, January 30, 1938. Postoperative, post-irradiation carcinoma of the right breast.

Treatment. The radiation was administered postoperatively at another institution. The therapy was initiated for swelling of the right neck, interpreted as metastatic nodes. Later treatment was given for residual thickening and swelling of the arm. Doses were massive.

Course. Slight cough and edema of the right arm were present before treatment. These increased markedly after therapy. Axillary pair now appeared. Roentgenograms of November 1937, showed right upper lobe fibrosis in the previously clear lung. The later films showed the same picture, also a fracture of the 3rd right rib posteriorly, without callus. The patient gives no history of trauma. At present. there is marked telangiectasia of the treated region and the right supraclavicular area is stony hard. The edema of the right arm is very marked, so that the extremity is useless. The lymphedema and skin changes are the outstanding features of this case; the lung symp toms are mild. The patient at present shows no evidence of malignancy.

Case VIII (Monte. Hosp. Rad. Cl. No. 5088). A. G., female, aged sixty-nine (Table VIII).

Status on Admission, December 13, 1937. Carcinoma of the right breast, excised locally; postoperative irradiation.

Treatment. The radiotherapy was administered at another institution and consisted of massive doses of 500-700 r to large fields. Course I was given before the local excision. Course II, after. Later courses were for edema of the breast, and prophylactically.

Course. The lungs were clear at the onset. By March 8, 1936, cloudiness of the left apex and widened mediastinum were noted. On February 17, 1930, report was "chest positive for metastases." These findings were evidently due

TABLE VIII

Year	Month	Field	Dose	Kv.	Ma.	Filter	Dist.
1924	4/4- 4/23 5/10	R. breast, R. axilla, R. lat. breast Single exposures Bare tubes implanted in R. axilla	700 r each 1650 mc-hr.	200		0.5 mm. Cu plus 1 mm. Al	50 cm.
1924	9/18- 10/7 12/2	Course 1 repeated, excluding radium therapy R. breast and axilla, lat.	700 F	200		o.5 mm. Cu plus 1 mm. Al	50 cm.
1925 111	3/10-	R. breast, lower; R. breast, lat.; R. breast, upper	700 r each	200		0.5 mm. Cu plus 1 mm. Al	50 cm.
1926 IV	1/18	R. axilla R. breast, R. axilla, R. supraclavicular	700 r 500 r each	200		0.5 mm. Cu plus 1 mm. Al	50 cm.
1927 V	1/1- 8/5	7 treatments, 500 r each, as follows: R. ant. supraclavicular—3 treatments R. ant. axilla—2 treatments R. breast—2 treatments	1500 r 1000 r 1000 r	200		0.5 mm. Cu plus 1 mm. Al	50 cm.
1928 VI	6/14	R. ant, breast	600 r	200		0-5 mi . Cu	50 cm.

#### TABLE IX

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1934	5/10	Gold seed implants, L. neck	and the second s	1000 mc-hr.				
1934 11	6/19- 6/25	L. supraclavicular, ant., post.; L. direct axilla, average R. supraclavicular, ant., post.; R. direct axilla, average	10 ×12 cm. 10 ×12 cm.	500 r each	198	30	o.5 mm. Cu. plus 1 mm. Al	50 cm.
1934 111	6/26- 7/4	Course 11 repeated	alling harmon constraints of the property of the second se		198	30	0.5 mm. Cu plus 1 mm. Al	50 cm.
1934 1V	7/5- 7/11	Course 11 repeated			198	30	0.5 mm. Cu plus 1 mm. Al	50 cm.
1934 V	11/28-	R. breast; R. axilla, post.; R. axilla, direct; and R. lower breast	77.7	600 r each	198	30	o.5 mm. Cu plus 1 mm. Al	50 cm.
1934	12/8-	Radium element pack, L. supraelavicular region		23000 mg-hr.				
1935 VI	3/12- 3/14	Radium element pack, L. infraclavicular region		24000 mg-hr.				The street of th
1935 VII	5/21- 5/22	L. upper breast, L. supraclavicular, post.		700 r each	198	30	0.5 mm. Cu 1 mm. Cu	50 cm.

to pneumonitis. At present, there is noted, on the right, fibrosis and large calcific plaques in the upper lobe, tenting of the diaphragm and pleural adhesions. The treated skin shows telangiectasia and induration, and a draining unhealed ulcer in the right axilla. The 2nd, 3rd, 4th and 5th right anterior ribs show old fractures with eburnation of the ununited ends, resulting in pseudarthrosis. No history of trauma. The fractured ribs give no pain. Since the last treatment, eleven years have elapsed without evidence of recurrence or metastases. The ulcer and pain in the right axilla, with restriction of arm motion, are her present chief complaints.

CASE IX (Montefiore Hospital No. 29398). N. B., female, aged fifty-six (Table IX).

Status on Admission, April 28, 1938. Postoperative, post-irradiation carcinoma of right and left breasts.

Treatments. All radiotherapy was given at another institution. Large massive doses were used, combined with gold seed implants. Courses II to v were prophylactic postoperative. The radium element pack was applied for residual disease.

Cours? Pain appeared in the left side of the neck at the completion of irradiation. The lungs were negative at this time. On April 19, 1938, there was noted some fibrosis in the infraclavic-

ular part of the left lung, destruction of the sternal end of the left clavicle with pathological fracture, fracture of the 2nd left anterior rib,

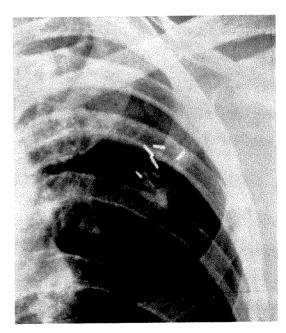


Fig. 8. Case IX. Few fibrotic infiltrations in the left infraclavicular regions. Pathological fracture with overriding of fragments medial third of left clavicle. Fracture of second left anterior rib with non-union.

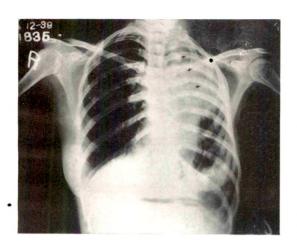


Fig. 9. Case x. Marked fibrosis left upper lobe. Trachea and mediastinum are drawn over to the left. Arrows point to areas of calcification in the supra- and infraclavicular regions in the anterior portion of the lung.

and osteoporosis of the 1st to 5th left ribs. The fractures are ununited. There are telangiectasia and induration of the left infraclavicular region. The patient presents no evidence of metastasis at this time. Both sides received approximately the same roentgen therapy; therefore, the addition of the gold seeds and the radium element pack to the left must be considered the cause of the lung and skin changes, fractures, etc., noted in this area.

Case x (Montefiore Hospital No. 15012). R. N., female, aged twenty-seven (Table x).

Status on Admission, July 9, 1927. Probable lymphoblastoma involving the left supraclavic-

ular and mediastinal nodes. Left pleural effusion.

Treatment. One treatment daily, dose 250–330 r. The last course was given because the pneumonitis was interpreted as recurrence.

Course. Dyspnea and weakness were present. on admission. Later, pain appeared in the left supraclavicular area, also morning cough and palpitation. The original films showed a left mediastinal mass and left pleural effusion. These disappeared following irradiation. A few linear infiltrations were noted on December 9, 1929. They became more marked by February 4, 1930, with the mediastinum drawn to the left. The fibrosis and adhesions showed further progression by October 1, 1930. Course IV was then given and was followed by increased fibrosis and calcific infiltrations in the left upper lobe. These have persisted for the past six years and, in addition, the trachea and mediastinum are pulled to the left and the left dome of the diaphragm is elevated. The roentgen picture of pneumonitis dates from December, 1929. At present, this patient's only complaint is moderate dyspnea on exertion.

Case XI (Monte. Hosp. Rad. Cl. No. 1773). Z. B., female, aged fifty-one (Table XI).

Status on Admission, March 31, 1931. Lymphoblastoma involving hilar nodes.

Treatment. Average dose 330 r. For the third course 200 r.

Course. Following the first course of irradiation, the hilar nodes became much smaller. Cough appeared one week and dyspnea six weeks following the second course. Roentgeno-

TABLE X

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1927 I	7/9- 7/30	L. chest, ant. L. chest, post. L. chest, lat. Mediastinum and R. chest, ant. Mediastinum and R. chest, post. L. supraclavicular, ant.	23 ×10 cm. 23 ×14 cm.	985 r 1315 r 985 r 985 r 985 r 985 r	200	5	o.5 mm. Cu plus 1 mm. Al	50 cm.
1929 11	I /2 I — I /3 I	R. supraclavicular, post.		1640 r	200	30	2 mm. Cu plus 1 mm. Al	50 cm.
1929- 1930 III	11/9-	L. chest, upper and medial R. chest, upper and medial lat.		1970 r 1970 r 1970 r	200	30	2 mm. Cu plus 1 mm. Al	50 cm.
1930 IV	10/11-	Ant. upper chest Ant. upper medial chest		1970 r 1970 r	200	30	2 mm. Cu plus 1 mm. Al	50 cm.

TABLE XI

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1931	3/3I- 4/28	R. ant. and post. chest L. ant. and post. chest Ant. and post. medial chest	20 ×14 cm. 20 ×14 cm. 18 ×15 cm.	985 r each 985 r each 985 r each	200	30	o.5•mm. Ag plus 1 mm. Al	50 cm.
1932	3/21-4/8	Ant. and post. chest	20 ×18 cm.	2000 r each	200	30	o.5 mm. Ag plus 1 mm. Al	50 cm.
1932	10/3-	R. ant. chest R. post. chest L. ant. and post. chest Ant. and post. mediastinum	20 × 16 cm. 20 × 16 cm. 20 × 16 cm. 20 × 10 cm.	400 r 200 r 200 r each 985 r each	200	4	o.5 mm. Cu plus I mm. Al	50 cm.
1934 IV	1/31-2/19	Post. medial chest	<b>22</b> ×25 cm.	1600 r	200	4	0.5 mm. Cu plus 1 mm. Al	50 cm.

grams now showed infiltrations suggesting fibrosis in the medial portions of both lungs. Five months later, these infiltrations were much more extensive, the diaphragm showed tenting and the heart was increased in size, the appearance suggesting pericardial effusion. Because the pneumonitis and resulting fibrosis were not recognized, the patient was given further irradiation. This was followed by recurrence of the cough, chest pain and increased dyspnea. In January, 1934, roentgenograms showed dense fibrosis with small calcific nodules in both upper lobes, extreme tenting of the diaphragm and mergence of the latter with the heart shadow. The heart was smaller. Later roentgen studies were unchanged. The patient's dyspnea was progressive and especially marked on exertion. Cyanosis and abdominal pain appeared late in the disease. The treated skin showed marked atrophy and telangiectasia. The patient died in June, 1939, with symptoms of right heart failure.

Postmortem Examination. This showed bilateral serosanguineous pleural effusions, marked bilateral thickening of the pleura, fixation and retraction superiorly of the diaphragm and dense adhesion to the anterior chest wall of the anterior mediastinal structures, the anterior pericardium and the root of the great vessels. The lungs presented atelectasis, hyalinizing fibrosis, intense congestion, areas of inflammation and areas with bronchial destruction. Heart failure cells were present in the alveoli. The heart showed marked thickening of the pericardial layers, hypertrophy and interstitial fibrosis of the right ventricle and extensive hyaline replacement with hypertrophy of the remaining fibers of the right auricle. The left

heart was normal. No evidence was found of lymphoblastoma.

CASE XII (Montefiore Hospital No. 27926). M. B., white male, aged thirty-nine (Table XII). Status on Admission, February, 1937. A case of Hodgkin's disease in the terminal stages.

Treatment. The roentgen therapy was administered at another institution. Courses I to IV were given for a mediastinal mass, supraclavicular nodes, a mass over the left chest wall and because of cough and shoulder pain. Courses V to VII were given for what was interpreted as Hodgkin's infiltration, though the findings on roentgen examination are those of pneumonitis.

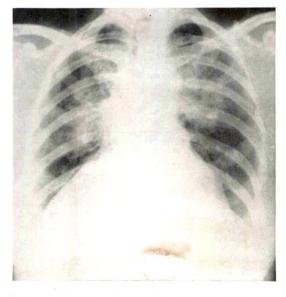


Fig. 10. Case XI. Soft infiltrations in the medial portions of the lungs. Tenting of the diaphragm.

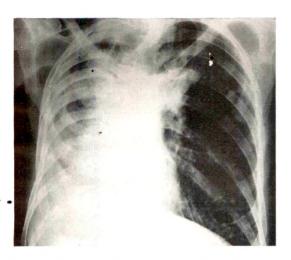


FIG. 11. Case XII. Trachea, heart and mediastinum drawn to right. Marked fibrosis of the right lung. Scattered areas of fibrosis left lung. Right diaphragm elevated.

The single doses were massive, as a rule 450-900 r per treatment.

Course. At the onset of his illness, the patient complained of cough and left shoulder pain. At this time, a mass was present at the right hilum, also a small right pleural effusion. These receded following irradiation. On April 24, 1934,

there was noted reappearance of the small right effusion, elight traction of the trachea to the right, and cloudiness of the lower half of the right lung. When admitted to Montefiore Hospital, there was present a productive cough, blood streaked sputum, dyspnea on exertion, and occasional rises in temperature. Roentgenograms of the chest now showed marked fibrosis of the right lung, retraction of the trachea and heart to the right, fibrosis in the left hilum and elevation of the right diaphragm. Cough and chest pain gradually increased. The patient later developed Cheyne-Stokes respiration, dyspnea, tachycardia and cyanosis. Death occurred on May 28, 1938.

Postmortem Examination. Right: The lung was small, fibrotic and airless; the pleura 0.75 cm. thick; the bronchi dilated and purulent. There were scattered patches of bronchopneumonia. The pulmonary arteries were arteriosclerotic. The veins of the hilum were partially or entirely occluded from without by granulation tissue. Left: The lung showed less severe but similar pulmonary changes. Heart: The pericardium was adherent. The right heart showed hypertrophy and dilatation of the auricle, ventricle and outflow tract. The left heart was negative.

TABLE XII

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1932 I	3/17-4/2	R. supraclavicular, ant. R. chest, ant. R. chest, post.	17 ×14 cm. 17 ×14 cm.	2700 r* 2700 r 2700 r	180	4	o.5 m.n. Cu plu 1 mm. Al	50 cm.
1933	5/18- 5/26	L. chest, ant.	16×14 cm.	2700 r	180	4	o.5 mm. Cu plus 1 mm. Al	50 cm.
1933	10/31	Entire chest, ant. Entire chest, post.		220 r 140 r	180	4	2 mm. Cu plus 1 mm. Al	80 cm.
1934 IV	1/23- 2/7	L. scapula R. scapula	14×14 cm. 7×9 cm.	4400 r 1200 r	180	4	1 mm. Cu plus 1 mm. Al	30 cm.
1934 V	4/27- 5/II	Entire chest, ant. Entire chest, post.		900 r 900 r	180	4	1 mm. Cu plus 1 mm. Al	75 cm.
1935 VI	2/27- 5/20	L. chest, ant. and upper Post. chest—very large field	10×15 cm.	400 r 300 r	180	4	2 mm. Cu plus 1 mm. Al	60 cm. 80 cm.
1936 VII	3/5-5/12	L. chest, ant. and upper L. chest, post. Entire chest, post.	Fields very large	800 r 1100 r 300 r	180	4	1 mm. Cu plus 1 mm. Al	50 to 80 cm.

<sup>\*</sup> r with back-scatter.

Microscopicall in addition to the extensive fibrosis, hyalinization, bronchial and vascular changes, there was a slight amount of Hodgkin's infiltration in both lungs.

Case XIII (Montefiore Hospital No. 28028). M. G., male, aged sixty-two (Table XIII).

Status on Admission, June 1, 1938. Carcinoma of the upper and middle third of the esophaous. Gastrostomy. Inactive pulmonary tuberculosis.

Treatment. At another hospital, 300 r to one field daily.

Case XIV (Montefiore Hospital No 28988). G. Z., female, aged forty-five (Table XIV).

Status on Admission, November 8, 1937. Postoperative carcinoma of the right breast.

Treatment. The irradiation was administered at another institution. Dosage was massive. Course IV was given because lung changes due to pneumonitis were interpreted as metastases. Extreme lymphedema necessitated a disarticulation of the right arm in 1934. The excised tissues were negative for carcinoma.

Course. The initial radiotherapy, two years after operation, was to a skin nodule in the

#### TABLE XIII

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1936	1/27- 2/28	R. ant. and post. mediastinum L. ant. and post. mediastinum		2700 r each 2700 r each	198	30	o.5 mm. Cu plus 1 mm. Al	60 cm.

Course. On admission, roentgenograms showed fibrotic infiltrations, due to healed tuberculosis, in the apices and infraclavicular regions. Marked fibrosis was also present in the medial port ons of both lungs (the field of irradiation), also pleurodiaphragmatic adhesions. Six months later, there was a marked increase in the pulmonary fibrosis, the right diaphragm was slightly elevated and the left diaphragmatic adhesions had disappeared. Calcifications were present in the right infraclavicular region. Onset, at about this time, of dry nocturnal cough and dyspnea on exertion. Three months later, there was an attack of hemorrhage, pain in the chest, dyspnea, cyanosis and rise in temperature. The patient died the next day with signs of bronchopneumonia.

Postmortem Examination. The lungs were normal in size. The medial portions were adherent to the mediastinum; the posterior portions to the posterior chest walls. In the region of the tracheal bifurcation, trachea, bronchi and aorta were matted together by fibrous tissue. Medially, the lungs were firm and fibrotic; laterally, the parenchyma was normal. The apices showed bilateral healed tuberculosis. Some of the bronchioles were widened and contained mucopurulent exudate. The left lower lobe was congested, slightly edematous, and contained areas of bronchopneumonia, Tuberculosis was found in the hilar lymph nodes. The parietal pericardium was firmly adherent on both sides to the pleura. Musculature of the right ventricle was slightly thickened.

right axilla. Dyspnea, chest pain and swelling of the right upper extremity had their onset in 1927, following the roentgen therapy. These increased with further irradiation. In April, 1928, infiltrations about the right hilum due to pneumonitis were interpreted as metastases and further irradiation was prescribed. Complaints and chest findings remained unchanged until 1936, when dyspnea and chest pain suddenly became marked. Roentgenograms now showed infiltrations in the right upper lung and a massive pleural effusion which on aspiration contained carcinoma cells. The skin and tissues of the right supraclavicular region and shoulder

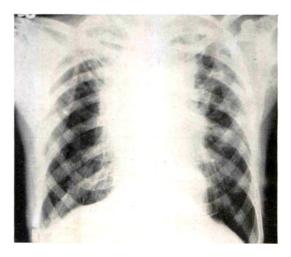


Fig. 12. Case XIII. Marked fibrosis in the medial portions of the lungs.

TABLE XIV

Year	Month	Field	Dose	Kv.	Ma.	Filter	Dist.
1927 I	5/16 · 5/17	R. axilla R. axilla, gold seeds implanted	600 r 460 mc-hr.	200	30	0.5 mm. Cu	50 cm.
	5/19-	R. chest, lower; R. chest, lat.	600 r each	140	4	4 mm. Al	30 cm.
	5/23	R. supraclavicular	600 r	200	30	o.5 mm. Cu	50 cm.
1927	8/2-	R. supraclavicular; R. axilla	600 r each	200	30	o.5 mm. Cu	50 cm.
II	8/5	R. chest, lat.	600 r	140	4	4 mm. Al	30 cm.
1928	1/23-	8 treatments, rotating fields					
III	4/3	R. chest, lower—2 treatments total	1300 r	140	4	4 mm. Al .	,;o cm.
		R. chest, lat.—2 treatments total	1300 r	140	4	4 mm. Al	30 cm.
		R. breast—2 treatments total	1100 r	200	30	o.5 mm. Cu	50 cm.
		R. axilla—2 treatments total	1100 r	200	30	o.5 mm. Cu	50 cm.
1928 IV	7/30- 8/6	R. chest, post.; R. supraclavicular; R. axilla, direct	500 r each	185	30	0.5 mm. Cu	50 cm.
1928 V	12/13	R. axilla, post.; R. supraclavicular, post.	500 r each	185	30	0.5 mm. Cu	50 cm.

presented marked telangiectasia and induration. Absorptive changes were present in the right scapula and upper ribs. The patient died on February 18, 1938. She represents a long-standing case of pneumonitis who developed metastases in the affected side eight years later.

Case xv (Montefiore Hospital No. 27640).

• G. R., male, aged sixty-three (Table xv).

Status on Admission, November 9, 1939. Carcinoma of the lower and middle third of the esophagus.

Treatment. Two to three fields treated daily with doses of 250-400 r per field. Esophagoscopy following first and third courses showed presence of an epithelitis.

Course. Dysphagia and pain in dorsal area appeared two months following the last course of irradiation. Roentgenograms showed increased hilar markings, slight fibrosis of adjacent right lung and a few infiltrations at the

right base. Gastrostomy performed. Films over the next seven months showed a dense infiltration in the medial portion of the right lung, increase in the infiltrations at the right base, elevation of the right diaphragm, left pleural effusion and suggestive pericard. I effusion. During this period, the patient developed marked dyspnea, clubbing of the fingers and râles at both bases. Bronzing and atrophy of the treated skin was present. The patient died nine and a half months following the last irradiation.

Postmortem Examination. Carcinoma of the esophagus with extension to the pleura and contiguous structures, but not to the lung. Marked fibrosis and thickening of the pleura. Extreme fibrosis and atelectasis, with areas of acute inflammation and bronchiectasis, in the medial portions of the lungs. Small effusion in the pericardium. Moderate hypertrophy and dilatation of the right auricle and ventricle.

TABLE XV

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1936	11/16-	Ant. and post. mediastinum R. ant. medial lung L. ant. medial lung	12 ×8 cm. 12 ×8 cm. 12 ×8 cm.	1600 r each 750 r 500 r	200	30	o.5 mm. Ag plus 1 mm. Al	70 cm.
1936	12/7-12/12	Ant. and post. mediastinum R. ant. medial lung L. ant. medial lung	12 ×8 cm. 12 ×8 cm. 12 ×8 cm.	1500 r each 400 r 550 r	200	30	0.5 mm. Ag plus 1 mm. Al	70 cm.
1936- 1937 111	12/29-	Ant. and post. mediastinum R. ant. medial lung L. ant. medial lung R. post. lung	12 ×8 cm. 12 ×8 cm. 12 ×8 cm. 12 ×8 cm.	1525 r each 550 r 650 r 400 r	200	30	0.5 mm. Ag plus 1 mm. Al	70 cm.

Case xvi (Montefiore Hospital No. 23973). L. K., male, aged fifty-two (Table xvi).

Status on Admission, September 19, 1933. Carcinoma of the lower third of the esophagus. Gastrostomy June, 1933.

Treatment. First course given elsewhere, 200 r per treatment. At Montefiore Hospital, second course, daily dose 330 r, third and and fourth courses, 250–300 r.

Corner. Following the second course of irradiation, the esophageal obstruction disappeared. Third and fourth courses of irradiation were given for recurring esophageal obstruction. Roentgenograms, six weeks following Course III, showed a partial consolidation of the right lower lobe, a few infiltrations at the left base and slight elevation of the right diaphragm. Severe cough appeared three weeks after the last irradiation. Roentgenograms now showed fluid at both bases. One month later, there was atelectasis of both lower lobes with a few infiltrations at the bases and an increase in the right pleural effusion. The patient declined rapidly and died on February 2, 1935, ten weeks following the last irradiation.

Postmortem Examination. Fixation and stenosis of the esophagus but no evidence of carcinoma. Large bilateral pleural effusions. Marked fibrosis and atelectasis of the lungs. Stroma filled with lymphocytes, macrophages and multinucleated giant cells. Vessels are thickened, edematous and almost all plugged with thrombotic masses. Some are partially organized. Bronchi are dilated. Heart presents a small hemorrhagic pericardial effusion, a thick white external pericarditis with adhesions to the pleura, and adhesion of the anterior surface to the pericardium.

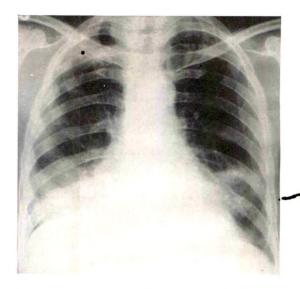


Fig. 13. Case xvi. Adhesive pericarditis (without cardiac enlargement as shown at postmortem). Atelectasis and fibrosis of right lower lobe, with some fibrosis of left lower lobe.

Case xvII (Montefiore Hospital No. 28032). S. S., female, aged sixty-two (Table xvII).

Status on Admission, October 22, 1928. Postoperative carcinoma of the right breast referred of for prophylactic irradiation.

Treatment. Average dose 330 r.

Course. Following the second course of irradiation, which was given to a recurrence in the right axilla, the patient became very susceptible to upper respiratory infections. Roentgenograms six months later showed slight atelectasis and haziness of the right lung and a few atypical infiltrations in the right upper lobe. The third, fourth and fifth courses of irradia-

TABLE XVI

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1933	May	Ant. and post. mediastinum	10×15 cm.	1600 r each	200	5	o.5 mm. Cu plus 1 mm. Al	50 cm.
1933- 1934 11	10/27- 1/6	Ant. and post. mediastinum R. ant. and post. chest L. ant. and post. chest	12 ×8 cm. 12 ×8 cm. 12 ×8 cm.	2650 r each 2650 r each 2650 r each	200	30	0.5 mm. Ag plus 1 mm. Al	50 cm.
1934	3/29-	Same fields as in Course II	12×8 cm.	2000 r each	200	30	o.5 mm. Ag plus 1 mm. Al	50 cm.
1934 IV	9/17- 11/23	L. ant. and post. chest R. ant. chest Post. mediastinum R. and L. lat. chest	12 ×8 cm. 12 ×8 cm. 12 ×8 cm. 10 ×15 cm.	2000 r each 2000 r 2000 r 2000 r each	200	30	0.5 mm. Ag plus 1 mm. Al	50 cm.

TABLE XVII

Year	Month	Field	Size	Dose	Kv.	Ma.	Filter	Dist.
1928 I	10/22- 11/12	R. ant. clest R. ant. and post. supraclavicular R. ant. axilla		985 r 985 r each 850 r	200	4	o.5 mm. Cu plus 1 mm. Al	40 cm.
1929 11	9/24- 10/15	R. direct axilla R. ant. axilla R. post. axilla R. ant. chest and axilla	12 ×9 cm. 14 ×10 cm. 13 ×8 cm. 14 ×20 cm.	2270 r 1650 r 330 r 650 r	200	30	o.5 mm. Ac plus 1 mm. Al	
1930	4/24- 5/9	R. ant. chest R. post. chest R. lat. chest	20 ×15 cm. 20 ×15 cm. 20 ×10 cm.	1025 r 955 r 985 r	200	30	o.5 mm. Ag plus 1 mm. Al	cm.
1930 IV	12/11-	R. ant. chest R. post. chest	16 ×24 cm. 15 ×22 cm.	985 r 750 r	200	30	o.5 mm. Ag 1 mm. Al	50 cm.
1931 V	3/4- 6/17	R. ant. chest R. post. chest R. upper and lower post. chest R. lat. chest	17 ×20 cm. 20 ×18 cm. 17 ×19 cm. 17 ×12 cm.	2300 r 1315 r 1315 r each 2300 r	200	30	o.5 mm. Ag plus 1 mm. Al	50 cm.

tion were given because irradiation changes in the right lung were interpretated as metastases. Dyspnea, cough, pain and cyanosis were severe following the fourth course. The right lung showed progressive atelectasis, increased infitrations and marked thickening of the pleura. The right thorax became markedly contracted and in 1932 a dense shadow replaced the right lung. The skin was now severely telangiectatic and there was also a woodeny infiltration of the right chest wall. Following Course v, fractures were observed in the right 2nd, 3rd and 7th anterior ribs, and in the 6th and 9th posterior ribs.

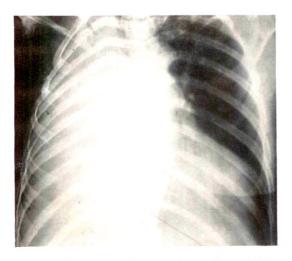


Fig. 14. Case xvii. Marked contraction of right chest. Right lung replaced by a very dense shadow. Third and 7th right anterior ribs and 6th and 9th posterior ribs show healed fractures.

The fractures subsequently united. Over a period of years, the liver increased enormously in size with no clinical evidence of metastases. She died in August, 1938, with symptoms of right heart failure.

CASE XVIII (Montefiore Hospital No. 23187). F. R., female, aged forty-five (Table XVIII). Status on Admission, October 18, 1933. Post-operative carcinoma of right breast.

Treatment. Irradiation, with the exception of the last course, was given at another institution. Dosage was massive. Course I was preoperative, Course II postoperative. Courses III and IV were given for "pulmonary metastases," diagnosed instead of pneumonitis. The average dose in the last course was 250 r.

Course. Chest pain and dyspnea began immediately after operation, November 4. 1932. By 1933, she already complained of orthopnea, weakness and night sweats. The lungs had been clear in 1932. A roentgenogram on March 2, 1933, showed on the right, pulmonic haziness with scattered soft infiltrations, especially in the medial portion, interlobar effusion and elevation of the dome of the diaphragm. By October, 1933, extensive fibrosis of the right lung and very thick right pleura were noted. In 1937, in addition, the trachea and mediastinum were markedly drawn to the right. The ribs on the treated side showed sharply delimited osteoporosis, irregularity of outline, and narrowing. The treated skin was telangiectatic and very indurated. Both lung and rib changes were sharply delimited and appeared directly beneath the dangiectatic skin areas. The symptoms of pneumonitis developed soon after operation, and the angle massive doses, rather than the total dosage, must be considered the cause. With further irradiation, the right arm and the beame painful. Cough and dyspnea In the later stages of this patient's mass, fever and hemoptysis were prompicated as on June 2, 1938.

I have Examination. The right lung was about a rulf normal size, the trachea adherent to the upper lobe and the pleura hard, gray and about I cm. thick. On section, the lung was fibrotic and the bronchi dilated. A thrombus was present in the inferior pulmonary artery. The left lung was voluminous. The heart showed a small pericardial effusion, a slightly hypertrophied right ventricle and dilatation of the pulmonic conus. The left heart was negative.

The microscopic examination showed, in the right lung, a hyalinizing fibrosis with lymphocytic infiltration, dilated bronchioles and occasional lung abscess formation. Congestion and edema were present in the left lung.

The postmortem examination was negative for recurrence or metastases.

#### ROENTGEN FINDINGS

Roentgen studies of the lungs in these patients, in the early stages of pulmonary reaction, reveal varying pictures of inflammatory changes. A common finding, at this time, is a haziness of the irradiated portion. This is soon followed by irregular patches of consolidation radiating out from the hilum. They are of uneven density and frequently coalesce. Such changes may



Fig. 15. Case XVIII. Extensive fibrosis of the right lung with marked thickening of the pleura. Right thorax is very contracted. Right ribs are narrowed, irregular in outline and show areas of osteoporosis and sclerosis.

manifest themselves after a few massive treatments or after a single intensive course of irradiation over fields of moderate size. When the irradiated fields are large, concomitant pulmonary and pleural reactions are the rule. In addition to the pulmonary consolidations above described, there are observed adhesions between the pleura and pericardium, and between the diaphragm

TABLE XVIII

Year	Month	Field	Dose	Kv.	Ma.	Filter	Dist.
1932	II/I II/2	R. breast ant., lower half; R. breast lat. R. breast ant.; upper half, R. axilla	700 r each 700 r each	198	30 30	0.5 mm. Cu 0.5 mm. Cu	50 cm
1933	I/2I- I/23	R. breast ant., lower half; R. breast lat.	530 r each	140	4	4 mm. Al	30 cm
	1/26	R. breast ant., upper half, R. axilla	750 r each	198	30	0.5 mm. Cu	50 cm
1933	3/2- 3/6	R. chest ant., upper half; R. chest post., upper half R. chest ant., lower half; R. chest post., lower half	800 r each 800 r each	198	3° 3°	0.5 mm. Cu 0.5 mm. Cu	50 cm.
1933- 1934 IV	11/6-	R. chest ant., lower R. chest post., lower Ant. mediastinum	1000 r total 1250 r total 750 r total	200	30	2 mm. Cu plus 1 mm. Al	50 cm

and pericardium or pleura, with tenting of the medial portion of the diaphragm. Pleural, pericardial and, less frequently, interlobar effusions are occasionally present. If no further treatment is given, and if the initial course has not produced extensive injury, the sole residue months later may be slight pulmonary fibrosis and a few pleural, pericardial and diaphragmatic adhesions.

The late stages of severe lung damage are dominated by a picture of fibrosis. The normal architecture of the lung may disappear. Atelectasis is common in the area of irradiation, with compensatory emphysema in the non-involved portions. The diaphragm, in many instances, shows numerous pleural and pericardial adhesions, resulting in tenting and some elevation. The heart and trachea are drawn over to the involved side. Pleural thickening occasionally is marked and, at times, will obscure lung markings. The thorax, as a rule, becomes markedly contracted. With the passage of years, in addition to the fibrosis, fairly large and sharply outlined calcific plaques may appear in the irradiated lung or pleura.

#### SKIN CHANGES

As one would expect, patients with lung damage of any extent, all show damage to the overlying skin. In a mild case, the late changes consist of some telangiectasia and slight atrophy. In more severe cases, atrophy and telangiectasia are marked and, in addition, brawny induration is a constant feature. At times, the skin induration and resultant contraction of the chest wall are striking. Where the axilla and supraclavicular region are severely involved, the underlying tissues may reach a stage of stony hardness so that it interferes with drainage.

Comparison of the roentgenograms and the photographs of the skin shows that the area of pulmonary involvement corresponds to the area of skin damage.

#### BONE CHANGES

In some instances, when the total dosage

is high, bone changes may be observed in the field of irradiation. These occur in patients surviving for long periods after treatment is given. Such changes manifest themselves as a rarefying osteitis. In the affected ribs are noted osteopore is observed circumscribed circular areas of oscerving narrowing of the ribs and irradiated ribs or contour. Fractures, in the above of clavicle. Such fractures frequently not unite. In time, eburnation of the ununited ends may take place, resulting in a type of pseudarthrosis. Where the bone displacement is slight, healing may be by bony union.

#### CLINICAL COURSE

Symptoms may present themselves before the pulmonary damage can be demonstrated by roentgen examination. The earliest signs are cough, usually non-productive and at times paroxysmal, slight dyspnea, and chest pain at the site of treatment. Fever and sweating may also occur. Where the damage is limited, these symptoms disappear following resolution of the pneumonitis.

Where the lung damage has been so extensive and severe that a permanent marked fibrosis is the result, the cough is persistent, the dyspnea progressive and especially marked on the least exertion, and the chest pain severe. Repeated upper respiratory infections, associated with chills, fever, heightened dyspnea and hemoptysis or streaking of the sputum, are also features of this stage.

After a varied period, which sometimes may last years, these severe cases go on progressively to a terminal stage. The symptoms now are predominantly those of right heart failure, including cyanosis, orthopnea, clubbing of the fin s, râles at the lung bases and, occasionally, an enlarged tender liver.

#### PATHOLOGY

Eight of the II patients who died had postmortem examinations. These were done six weeks to eight years following the onset

of the irradiction. The histological changes check very closel, with those obtained in animal experiments.

Macroscopical, the irradiated portions of the lungs were atelectatic, firm in constance and cut with increased resistance.

The lungs were atelectatic, firm in constance and cut with increased resistance.

The lungs were at lungs, showed obliteration of the lungs and extreme thick and a printing to I cm., were observed.

Occ. The lungs were adherent to the medias man and to the chest walls. In one patient, the two main pulmonary veins were almost completely occluded by granulation tissue. Another showed the trachea, pronchi and aorta matted together by fibrinous tissue.

Microscopically, inflammatory changes were found in the lungs and pleura. Where the irradiation was of long duration, severe fibrosis and hyalinization were present. In these patients, dilatation of the bronchi, bronchiectasis and bronchitis were also noted. Persisting alveoli were small and frequently filled with inflammatory exudate. Areas of edema, hemorrhage and necrosis were observed in the acute cases. Atherosclerosis of the pulmonary arteries, thickening, edema and thrombosis of the pulmonary vessels, and thrombosis of the inferior pulmonary artery were also present.

Changes in the heart were striking. Hypertrophy, or dilatation of the right side, was present in 6 cases; the 2 cases that did not show this finding ran an acute course and died one to two months following the appearance of pneumonitis. In no case was there enlargement of the left heart. Pericarditis and parietal pericardial adhesions were observed in 4 instances. Four patients also showed small associated pericardial effusions. Perivascular fibrosis of the heart vessels was found on one occasion.

#### MECHANISM OF RIGHT HEART FAILURE

As stated previously, the terminal picture of many of these patients with extensive radiation fibrosis, is one of right heart failure. The mechanism of this type of cardiac impairment is of considerable interest.

It has been described in comparable lung conditions where marked infiltration of lung, bronchi and pleura serve to interfere seriously with the pulmonary circulation as, for example, in chronic pulmonary tuberculosis, of the fibroid type, and also in emphysema heart. As the fibrosis progresses, the capillary beds of the lungs become narrowed, and increased resistance results, i.e., hypertension of the pulmonic or lesser circulation. Enlargement and hypertrophy of the right heart then follow.

In these conditions, as in the postmortem findings previously cited, coronary artery disease was not seen. The exceptional pleural thickening, which was present in several of our patients, may have acted as a contributory factor. In those cases where the mediastinum was the seat of a dense fibrotic process, which surrounded bronchi, trachea and aorta, and even constricted the pulmonary veins, a direct interference with pulmonary circulation can be inferred.

With the establishment of pulmonary hypertension, there follows the train of compensatory events which is the basis for the clinical picture. These sequelae are increased venous pressure in the pulmonic circulation, marked lung congestion leading to hemoptysis, enlarged right heart and dilatation of the pulmonic conus, accentuation of the pulmonic sounds, enlargement of the liver, cyanosis and finally infarction of the lungs.

The right heart enlargement, observed at postmortem, was not easily discernible on the roentgenograms. Many of these cases originally had masses extending along the mediastinum and hilum or later, following irradiation, developed extensive hilar fibrosis, pericarditis and adhesions, and cardiac displacement. These changes alter the cardiac outlines markedly and make finer interpretation dubious.

While electrocardiograms exist for some of our patients, none were taken prior to irradiation, and the findings available are varied. It is hoped that in the future, reliable criteria can be assembled for such cases.

#### COMMENT

We do not possess, as yet, precise knowledge of the quantitative relationship of dosage to radiation pneumonitis. Therefore, no simple dosage formulas for lung irradiation can be offered, which will prevent its occurrence. Moreover, in treating thoracic malignant neoplasms, it is not always desirable to use dosages which will completely avoid this type of injury. First, because dosages must be applied which are bound to inflict some lung damage, if a real attempt to control the malignant condition is made; and second, because a limited degree of pneumonitis produces little in the way of symptoms or permanent functional impairment.

As was noted in the series of cases presented here, it is only severe radiation damage to a large portion of the lung and mediastinum which produces intolerable after-effects. The occurrence of severe injury should be borne in mind, so that treatment may be planned to avoid it. The following points, we believe, will prove of value in the prevention of major radiation damage:

- 1. The lung damage will appear under the portion of the chest wall that is most heavily irradiated and, where crossfire technique is used, in the region where the beams cross.
- 2. Massive doses, especially if repeated, and at close intervals, are likely to produce such injuries, even if the total dosage is not high, judged by today's standards. In these instances, it is not the total dosage which is the determining factor, but the amount given per treatment.
- 3. Irradiation which is limited to the lung periphery is less likely to produce serious injury than heavy irradiation over the mediastinum and large vessels.
- 4. Previous therapy, although no injury resulted with the earlier series, can be the basis for later damage, if subsequent treatment is not given with great caution.
- 5. If the primary therapy has resulted in some radiation pneumonitis, the likelihood of severe damage is great if addi-

tional therapy is given to surfareas. The possibility is greater if large fields are used.

- 6. Where large fields are used, and marked skin changes occur, the possibility of such a lesion should be kept in mind and a careful watch kept for early signs.
- 7. Elderly individuals, with arteriorderotic changes, must be considered more likely to have such damage.
- 8. Respiratory symptoms, such accough, dyspnea and chest pain, are danger signals.
- 9. A diagnosis of pulmonary metastases must be accepted with reservation, when heavy dosage has been given, if based on changes found only in the part of the lung corresponding to the area of treatment:
- 10. Repeated roentgen studies of the lung during and following treatment will call attention to pulmonary damage in its incipient stages and will help differentiate this condition from metastases.

To conclude, the radiologist will find his best protection in avoiding lung damage, or at least limiting its extent, in the constant awareness of the conditions under which it occurs, and in the possibility of its occurrence in extensive irradiation over the thorax.

#### REFERENCES

- I. Bergonié, J., and Tessier. Rapport sur l'action de rayons X sur la tuberculose. Arch. d'électric. méd., 1898, 6, 334-360.
- 2. Davis, K. S. Intrathoracic changes following x-ray treatment; clinical and experimental study. *Radiology*, 1924, 3, 301–322.
- 3. Desjardins, A. U. Certain unusual features noted in a case of inoperable cancer of the breast treated by roentgen rays. *Med. Clin. North America*, 1923, 7, 163–171.
- 4. Desjardins, A. U. The reaction of the pleura and lungs to roentgen rays. Am. J. Roentgenol. & Rad. Therapy, 1926, 16, 444-453.
- 5. Desjardins, A. U. Action of roentgen rays and radium on the heart and lungs. Am. J. Roent-genol. & Rad. Therapy, 1932, Vols. 27 and 28.
- 6. Downs, E. E. Lung changes subsequent to irradiation in cancer of the breast. Am. J. ROENTGENOL. & RAD. THERAPY, 1936, 36, 61-64.
- ENGELSTAD, R. B. Experimental investigations of lung changes following röntgen radiation. Acta radiol., 1933, 14, 655-656.

- 8. ENGELST, R. B. Ueber die Wirkungen der Röntgeristrahlen auf die Lungen. *Acta radiol.*, suppl. 19, 1934, pp. 1–94.
- 9. ENGELSTAD, R. B. Die Strahlenreaktion in dem Lungen beim Menschen. *Acta radiol.*, 1937, 18, 32-43.
- io Evans, W. A., and Leucutia, T. Deep roentgen therapy of neoplastic pulmonary metastases. Am. J. Roentgenol. &. Rad. Therapy, 1924, 11, 35-50.
- II. Evans, W. A., and Leucutta, T. Intrathoracic changes induced by heavy radiation. Am. J. ROENTOENOL. & RAD. THERAPY, 1925, 13, 203-220.
- 12. Flaskamp, W. Sonderb. d. Strahlentherapie, 1930, Vol. 12.
- 13. GROOVER, T. A., CHRISTIE, A. C., and MERRITT, E. A. Observations on the use of copper filter in roentgen treatment of deep-seated malignancies. South. M. J., 1922, 15, 440-444.
- 14. Groover, T. A., Christie, A. C., and Merritt, E. A. Intrathoracic changes following roent-gen treatment of breast carcinoma. Am. J. Roentgenol. & Rad. Therapy, 1923, 10, 471-476.
- 15. GROOVER, T. A., CHRISTIE, A. C., MERRITT, E. A., and Coe, F. O. Roentgen pleuropneumonitis. South. M. J., 1927, 29, 153-158.
- 16. HARTMAN, F. W., BOLLIGER, A., DOUB, H. P., and SMITH, F. J. Heart lesions produced by the deep x-ray; experimental and clinical study. Bull. Johns Hopkins Hosp., 1927, 41, 36-61.
- 17. KARLIN, M. I., and MOGILNITZKY, B. N. Zur Frage nach der Wirkung der Röntgenstrahlen auf die Lungen und das Herz der Tiere. Frankfurt. Ztschr. f. Path., 1932, 43, 434-447.
- 18. KÜPFERLE, L. Experimentelle Studien zur Röntgenbehandlung der Lungentuberkulose. Fortschr. a. d. Geb. d. Röntgenstrahlen, 1914, 21, 85-89.
- KÜPFERLE, L., and BACMEISTER. Experimentelle Grundlagen für die Behandlung der Lungentuberkulose mit Röntgenstrahlen. Deutsche med. Wchnschr., 1916, 42, 96-99.

- 20. LÜDIN, M., and WERTHEMANN, A. Lungenveränderungen nach experimenteller Röntgenbestrahlung. Strahlentherapie, 1930, 38, 684-
- 21. Mctatosh, H. C. Changes in lungs and pleura following roentgen treatment of cancer of the breast by prolonged fractional method. Rediology, 1934, 23, 558-566.
- 22. QUADRONE, C. Zentralbl. f. inn. Med., 1905, 26,
- 23. Rudis-Jieinski, J. Electrochemical action of x-rays in tuberculosis. New York M. J., 1902, 7.5, 364-367.
- 24. STRASSER, ALOIS, Pleuritis nach Röntgenbehandlung eines Mediastinal Tumors: Zischrift. prys. u. diātet. Therap., 1912, 16, 65-70.
- 25. TSUZUKI, M. Experimental studies of the biological action of hard roentgen rays. Am. J. RDENTGENGL. & RAD. THERAPY, 1926, 16, 174-150.
- 26. TYLER, A. F., and BLACKMAN, J. R. Effect of heavy radiation on the pleura and lungs. J. Radiol., 1922, 3, 469-475.
- 27. WARREN, S. L., and WHIPPLE, G. H. Roentgenrey intoxication. I. Unit dose over thorax negative—over abdomen lethal. Epithelium of small intestine sensitive to x-rays. J. Exper. Med., 1922, 35, 187-202.
- 28. WARTHIN, A. S., and Pohle, E. A. Effect of reentgen rays on the heart. *Arch. Int. Med.*, 1929, 43, 15-34.
- 29. WIFTZ, H. Röntgenschädigungen in der Tiefentherapie. Forschr. a. d. Geb. d. Röntgenstrahlen, 1922, 30 (Kong. Heft), 133-138.
- 30. WIFTZ, H. Injuries from roentgen rays in deep therapy. Am. J. Roentgenol. & Rad. Therapy, 1923, 10, 140-147.
- 31. Wirtz, H. Erfahrungen in der Röntgenbehandlung des Karzinoms. Fortschr. a. d. Geb. d. Köntgenstrahlen, 1926, 34, 373.
- 32. WO-ILAUER, F. Der Einfluss der Röntgenstrahlen auf das Lungengewebe. Deutsche med. Wchnschr., 1909, 35, 1704-1706.
- 33. Zwer, H. G. Die theoretischen, experimentellen, klinischen und wirtschaftlichen Grundlegen der protrahiert-fraktionierten Röntgenbestrahlung maligner Tumoren. Strahlentherapie, 1932, 43, 201-248.



# THE EFFECT OF VISIBLE LIGHT ON THE DEVELOPMENT OF TUMORS INDUCED BY PARENE IN THE SKIN OF MICE\*

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#### INTRODUCTION

light on the skin of mice painted with tene are to be found in the literate. Poniach and Mottram<sup>2</sup> report that ce. An earcinogenic agents, including benzpyrene, sensitize the skin of animals to visible light. On the other hand, Taussig, Cooper and Seelig could report no very significant difference between painted mice kept in the dark, and those exposed daily for one hour to an electric sun lamp.

Clark, in a recent review, has suggested the possibility of a double action of radiation on the skin—one a sensitization to visible light, and also a carcinogenic effect of ultraviolet radiation, roentgen rays and radium. The preliminary experiments reported here were undertaken to investigate the effects of benzpyrene on mice kept throughout the experiment in an environment of (a) complete darkness, (b) twelve hour daily exposure to visible radiation.

#### EXPERIMENTAL PROCEDURE

The mice were kept in rooms, the construction of which has been fully described by Jones and Tuttle.<sup>3</sup> Forty mice of the Swiss Albino, Bar Harbour strain, were kept in Room I (complete darkness) and 40 in Room III (visible radiation). The mice were five to six months old at the beginning of the experiment. They were fed purina dog chow and distilled water; males and females were represented equally in each group, and segregated to prevent breeding.

Fluorescent lamps were substituted in Room III for the 1,500 watt tungsten lamps used before. Two types of lamps† were used, the "daylight" and the "blue" of the General Electric

† The spectral characteristics of these lamps has been described by G. E. Inman in "Characteristics of Fluorescent Lamps." Tr. III. Eng. Soc., 1939, 34, 65. Company, both of them the 36 inch, 30 watt type. They were fitted, one blue and one daylight alternating, at the base of the duct and operated for twelve hours daily at a distance of 4 inches above each cage—a total of 20 lamps was used. The illumination, on the working plane, was 300 foot-candles at the start; this dropped, at the end of six months, to 200 footcandles with aging of the lamps. The total energy was of the order of 0.1 gm/cal/cm<sup>2</sup>/min. of which about 10 per cent is in the far infra-red and about 5 per cent of wave lengths between 3,600 Å and 4,000 Å. We used the extra blue lamps because benzpyrene absorbs strongly in the blue region. The therapeutic and carcinogenic range of ultraviolet radiation was not present in the sources used.

The mice were painted twice weekly, in the interscapular region with 0.5 per cent solution of 3;4 benzpyrene in benzene and without previous epilation. A No. 8 camel's hair brush was used. A total of 35 paintings was given over a period of seventeen weeks. The mice were observed for sixty days after this. The experiment lasted from May 10 to November 10, 1939.

#### RESULTS

The results are given in Table 1.

We observed a marked difference in the reaction of the mice in the two rooms to the first few paintings. After only 4 paintings 93 per cent of the total in the light room showed definite bald patches, while only 59 per cent of those in the dark room showed any sign of baldness. The animals in the light room tended to stay bald, appeared to lose weight and showed a more marked constitutional reaction to the carcinogen at the start.

The means with their standard errors show no significant difference in the length of the latent interval to the development of the first papilloma between the two groups.

<sup>\*</sup> From the Department of Surgery and the Department of Zoology, University of Rochester, Rochester, N.Y. Aided by a grant from the Committee on the Effects of Radiation upon Living Organisms, Divisions of Biology and Agriculture, National Research Council.

It was observed, however, that in 6 cases of the group in the light, papillomata disappeared; in no case did this happen in the dark room group. A significant lengthening is seen in the light room group, of the latent interval to the development of the first carcinoma, also a significant lengthening of the interval from papilloma to carcinoma. The incidence of cancer, by pathological ciagnosis, was 79 per cent in the dark room, and

shows that the production of such tumors can be accelerated by the continuous certain oils. The new man oil Particles authors found, in agreement with the results on bearpyrene of Taussig, Cooper and Seelig, no effect of ultravioletting activity of a carcinogen, 1;2,556 disherant thracene. Our results indicate the radial

Table I

EFFECT OF LIGHT AND DARKNESS ON THE DEVELOPMENT DF SKIN TUMORS BY 3;4 BENZPYREN

	Et	Papillomata			Carcinomata					Ca per cent	
		No. mice with	Total No.	No. per mouse	Latent interval to 1st	No. mice with	Total No.	No. per mouse	Latent interval to 1st	Interval from 1st pap-ca.	_
Room 1, dark	38	37	111	2.9	III ±4.7 days*	30	58	1.5	144 ±4.7 days	35 ±3.2 days	79
Room III, light	34	29	72	2.1	121 ±5.2 days	15	28	0.8	168 ±4.3 days	56±7.3 days	44

Et = Effective total, number of mice that did not die before the appearance of the first papilloma.

\* This and all following errors = standard errors.

only 44 per cent in the light room groups. Taken together, these results indicate a retardation of the carcinogenic process, as well as a diminution in the number of animals affected, in the group exposed to light. The animals in the light room group that did not develop tumors were killed at the same time as the others and appeared healthy at autopsy.

The tumors found on microscopic examination of tissue were mostly of the squamous cell carcinoma type. In 2 cases, one in each room, a fibrosarcoma was found. One lung adenoma was found (dark room group) and one mediastinal lymphoma (light room group). The spleens in most cases were enlarged and showed hyperplasia and congestion; in 2 cases, one in each room, marked hyaline degeneration.

#### DISCUSSION OF RESULTS

Recent work of Rusch, Baumann and Kline<sup>4</sup> on tumors, produced by intense ul-

tions in visible light, from which ultraviolet radiations have been excluded, have some influence on the carcinogenic action of benzp=rene. It was, however, evident to us that in the early stages of the experiment the "light room" group were showing constitutonal changes at a time when the "dark\_room" group showed very little reaction to the carcinogen. Since, in the opinion or some workers, more tumors will occur in healthy stock than in stock physically below par, the higher percentage of tumors in our mice deprived of light can possibly be explained as tumors developing in a better nourished animal. If this difference in nutrition were not a factor, we might suspect either that radiation had changed the carcinogenic activity of benzpyrene, or else, by sensitizing the skin, produced a more resistant medium. If the latter were true it would seem that the effect of rad ation in visible light may differ from known carcinogenic effects of ultraviolet.

The matter is being investigated further using mice of other strains.

#### · CONCLUSIONS

Two groups of mice, of the Swiss Albino strain, were painted twice a week with 3;4 benzpyrene for seventeen weeks to induce skin tumors. One group was kept, throughout the experiment, for twelve hours daily in an environment of visible light, the other in complete darkness. A retardation of the carcinogenic process, and a diminution in the number of animals which developed tumors was found in the group exposed to light. It is suggested that radiations in visible light may differ, in their effects on the skin, from known carcinogenic effects of ultraviolet.

We wish to thank Dr. G. B. Mider for kind colla-

boration and much valuable help dure the conduct of the experiment. Our thanks are also due to Dr. Clifton Tuttle for supplying data on wave length limits of lamps, values for illumination, and energy equivalents of the radiations used.

#### REFERENCES

I. CLARK, J. H. Biological effects of radiation. Ann. Rev. Physiol., 1939, 1, 21-40.

2. Doniach, I., and Mottram, J. C. Sensitization of the skin of mice to light by carcinogenic agents. *Nature*, 1937, 140, 588.

3. Jones, L. A., and Tuttle, C. Isolation of desired qualities of radiant energy for biological experimentation J. Nutrition, 1939, 18, 611.

4. Rusch, H. P., Baumann, C. A., and Kline, B. E. Effect of local applications on development of ultraviolet tumors. *Proc. Soc. Exper. Biol.* Med., 1939, 42, 508.

5. TAUSSIG, J., COOPER, Z. K., and SEELIG, M. G. Effect of light on benzpyrene cancer in mice. Surg., Gynec. & Obst., 1938, 66, 989-993.



## FURTEER STUDIES ON THE ACTION OF ROENTGEN RAYS ON THE GAMETES OF AFBACIA PUNCTULATA\*

### I. DELAY IN CELL DIVISION CAUSED BY EXPOSURE OF SPERM TO ROENTGEN RAYS

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THAS been shown previously 1,2,3,4, that (I) exposure of sperm or eggs (or both) of Arbacia punctulata to hard roentgen rays before fertilization causes a delay in the occurrence of the first cleavage, that (2) increased exposure causes increased delay, that (3) no delay is caused by comparable doses when cytoplasm alone is treated, and that (4) recovery from the effect may occur before fertilization when eggs are treated but not when sperm are treated. With the exception of point (3) these results have been repeated and confirmed by Miwa, Yamashita and Mori<sup>5</sup> using the related form Pseudocentrotus depressus and found to be true also when beta or gamma rays are used in place of roentgen rays.

It is the purpose of this report to examine more critically the relation between dose of radiation administered and the amount of delay in cell division observed and to analyze the nature of the reaction in the light of the more recent findings.

#### MATERIAL AND METHODS

For the present work sperm alone were treated. This was done in order that the complicating factor of recovery, which enters in when eggs are treated, might be avoided. Eggs and sperm were collected in the usual way and "dry sperm" (i.e. exuded sperm material not diluted with sea water) was exposed in amounts of one or two small drops in thin walled celluloid pill boxes.

The roentgen-ray equipment used was the dual-tube self-rectifying outfit available at the Marine Biological Laboratory, a simultaneous cross-firing technique thus being used. The secondary voltage was 1947 kv. and the tube current on each tube was 25 me. The output intensity (as measured in air with a celluloid thimble type ionization chamber) at the point of treatment and after the radiation had passed through the heavy glass of the tube walls and 5 mm. of bakelite of the tube shields (equivalent inherent filter: 0.2 mm. copper) was 7,800 roentgens per minute. The distance from the center of each target to the center of the test material was 9.5 cm.

The exposure times were o (controls), 1, 2, 4, 8, 16, 32 and 64 minutes, the timing. being carried out and the conditions mentioned above being maintained as precisely as possille. At the end of each exposure, a portion of the treated sperm material was removed diluted properly with sea water and allowed to fertilize normal eggs. The cleavage time—that is, the time intervening between the moment of insemination and the moment when some particular percentage had divided—was then carefully determined in accordance with procedures previously described. For the experiments reported Fere, the times when various percentages of cleavage occurred were recorded. Moreover, an attempt was made to note the time when the first cell divided in each sample and also the time when the first ten had divided. The times of the first and the first ten cleavages in the samples did not beæ a precise relation to the times

<sup>\*</sup> The work to be reported in this series of papers was carried out mainly at the Manne Biological Laboratory, Woods Hole, Mass. Part of it was done while the author was connected with the Memorial Hospital, New York City, and the remainder since transferring to the National Cancer Institute. The microscopical sections and part of the drawings used here were prepared by Mr. Joseph C. Bender whose services were provided by the Memorial Hospital. The author is indebted to the Memorial Hospital for support of the early part of the work and to the Marine Biological Laboratory for use of its excellent sacilities.

when various percentages had cleaved since the number of individuals in the samples was not the same, but they did serve to indicate whether a w of the individuals escaped irradiation effect entirely.

#### RESULTS

The results for a typical experiment are given in Table 1 and plotted in Figure 1, the

will be noted (1) that in accold with what has been described previously, there is a general delay in the occurrence of cleavage and that this becomes greater as the amount of treatment administered is increased; (2) that among the controls cleavage occurs in practically all of the cells at the same time as indicated by the steep slope—almost vertical character—of the

TABLE I

C1	Minutes' Cleavage Time								
Cleavage	Ist	10th	10%	30%	50%	70%	90%	98%	
din. Exposure									
o (Control)		-	<b>4</b> I	41 ½	42	421	43	45	
1	54	67	82	84	85	87	89	95	
2	65	81	98	104	108	110	113	119	
4	66	99	123	127	130	135	139	143	
8		99	150	154	157	159	162	169	
16	115	151	175	182	185	188	194	207	
32	146	167	194	204	211	215	222		
64	-	_	_					******	

first and second points on each curve (Fig. 1) indicating the time of the first and first ten cleavages in each case, respectively. It

curve; (3) that in the irradiated samples cleavage occurs less uniformly among the cells, as indicated by the decrease in steep-

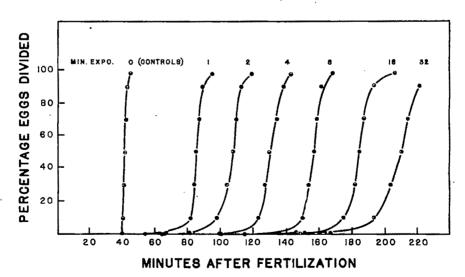


Fig. 1. Curves showing the percentage of eggs divided at various times after fertilization when different doses of roentgen rays are administered to the sperm before fertilization. (The first and second points in each case, however, are not based on percentage of eggs cleaved, but rather the times of the first and first ten cleavages, respectively.)

ness of the curves, but whereas a few of the cells cleave much earlier and some much later than the rest, most of them nevertheless divide at nearly the same time; (4) that none of the functional sperm fail to carry irradiation effect (as manifest by cleavage delay) into the eggs; and (5) that all of the eggs were successfully fertilized when the roentgen treatment did not exceed thirty-two minutes' exposure (250,000 r approximately).

In view of the fact that most of the eggs in a sample cleaved at about the same time. the moment of 50 per cent cleavage may be taken as most representative in each case. Such values as read from the curves (Fig. · 1) are 42, 85, 108, 131, 157, 185 and 210 minutes, respectively, for samples receiving o (control), 1, 2, 4, 8, 16 and 32 minutes' exposure. Subtracting the value for the control from those for the irradiated samples to obtain the actual minutes' delay caused by the treatment, the following figures were obtained: 43, 66, 89, 115, 143 and 168. These are plotted in Figures 2 and 3 to show how the irradiation effect (delay in cleavage) varies with dose of radiation (dose-effect curves).

It will be seen (1) that the curve (Fig. 2) rises rapidly at first but tends to become

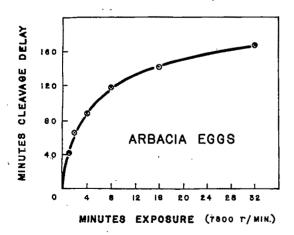


Fig. 2. Curve showing the minutes cleavage delay in fertilized *Arbacia* eggs whose sperm had received various exposures to roentgen rays before fertilization.

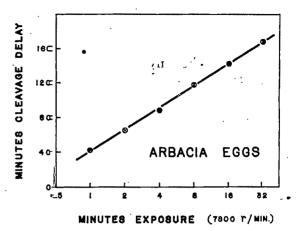


Fig. \_. Same as Figure 2, semi-logarithmic plot.

flattered, and (2) that a perceptible threshold effect is indicated only by the semi-logarithmic plot (Fig. 3). Thus the die-away character of the reaction suggests that something is being used up or destroyed by the radiation, and the close fitting of the experimental points to the exponential type of curve suggests that the reaction must be controlled by a single substance. The possible meaning of these suggestions will be dealt with further below.

Thus far only a single experiment has been Escribed. However, after a variety of exploratory tests had been performed, ten experiments of the type described above were carried out on different days and on different collections of material under as nearly the same conditions as possible. Briefly, it may be said that the same kind of deley was observed in every case and that the same type of dose-effect curves were obtained, these varying only in slope. Figure- 4 and 5 show the most extreme variations in slope observed.

#### DISCUSSION

It is \_nstructive to compare the response of the sea urchin material to roentgen rays with that of the photographic plate to light (Table II).

Exposure of the photographic plate to light produces a latent image which be-

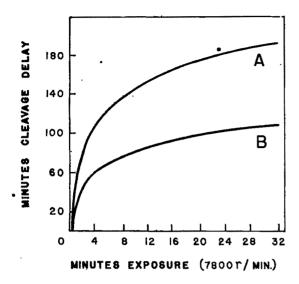


Fig. 4. Curves showing the minutes cleavage delay in fertilized eggs whose sperm had received various exposures to roentgen rays before fertilization. Curve A is for the most sensitive collection of material used, and Curve B for the most resistant.

comes manifest only upon development (photographic), the intensity of which varies directly with the logarithm of exposure to light over the major portion of the range of the reaction (in particular cases) (Fig. 6). Similarly, exposure of the sea urchin gametes to roentgen radiation produces a latent effect which becomes manifest only upon fertilization and the amount of effect (cleavage delay) is found to vary directly

TABLE II

Points Compared	Sea Urchin Material	Photographic Plate			
Treatment	Exposure to roentgen rays	Exposure to light			
Unobserved result	Latent effect (delay)	Latent image			
Demonstra- tion of re- sult	Fertilization and determination of cleavage time	Photographic de- velopment			
Observed result Degree of effect	Delay in cell di- vision Amount of delay varies directly with log dose	Photographic image Density of plate likewise varies directly with log dose			

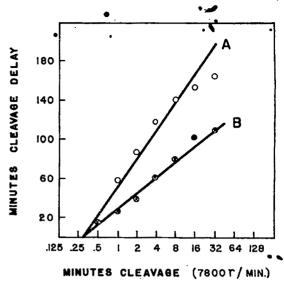


Fig. 5. Same as Figure 4 with experimental points shown—semi-logarithmic plot.

with the logarithm of exposure to roentgen radiation over the greater range of the reaction.

In case of the photographic plate, it is known that light acts upon the photographic emulsion causing metallic silver to be deposited when the plate is developed, and

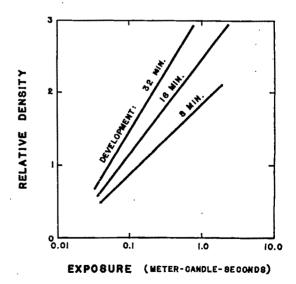


Fig. 6. Curves for 8, 16 and 32 minutes' development times, showing the relative density (degree of blackening) produced in a photographic plate for various exposures to light. (Data from Hardy and Perrin.)

further, that the density (the degree of blackening) is directly proportional to the amount of silver deposited per unit area of the plate. From this it is clear that the slope of the curve (Fig. 6) characterizes the rate at which silver is transformed by the light for any given development time. To what extent the response of the sea urchin gametes is like that of the photographic plate in these respects is not yet evident, but knowledge of the somewhat better understood photographic reaction has served to influence analysis of the gametic response.

By purely subjective reasoning, it is clear that in case of the living test objects the same as in case of the photographic rlate, radiation acts on some substance (or substances), which for the sake of simplicity may be called (x), and that as (x) is used up or changed, certain photo-products (p)must be formed from (x). Moreover, from the work with non-nucleated egg fragments and the fact that cleavage delay may be caused by irradiating sperm alone, it appears that (x) is most likely a nuclear zonstituent. In case of the photographic plate, it is clear that darkening of the plate is caused by a photo-product (p)—that is, by silver being deposited, but in case of the gametes no evidence is yet available to indicate whether loss of (x) or the formation of (p) is responsible for the effect observed. The question at this point, therefore, becomes resolved into one of whether roentgen rays destroy a substance in the nucleus which acts under normal circumstances to keep the mitotic schedule "on time" or whether they cause a new substance (p) to be produced which acts to slow the mitotic schedule. Because of the complex nature of the living system, the loss of some essential substance seemed as likely to be responsible for the effect observed as the formation of some toxic photo-product. Although the findings were negative, it is of interest at this point to mention a search for evidence of (p).

In previous experiments dealing with the recovery phenomenon, it was observed that 80 to 90 per cent of the recovery which oc-

currec took place within the first hour after treatment ceased. Further, it was observed that the curve showing loss of effect (recovery) as a function of time resembled the exponential type very closely. Considering the significance of these facts it seemed that the rate of recovery was too slow to be characteristic of the recombination of ions produced by the radiation and too fast to be characteristic of biological repair in the healing sense. The rate, however, did seem about right for the diffusion out or loss of a toxic photo-product such as (p) above, thus giving some reason for expecting that (p) might be demonstrated.

A heavy suspension of eggs with barely enough sea water to cover them was exposed o large doses of radiation (50,000 r). Following treatment the eggs were allowed to stand in the treated sea water for an hour, at the end of which time the supernatant fluid was removed and placed over fresh r-on-irradiated eggs. One hour later these eggs were fertilized and their cleavage time determined. It was expected that if (p) diffused out of the irradiated eggs into the sea water medium, it might in a similar manner diffuse back into the fresh eggs enough to cause a detectable delay. As intimatec above, the results were entirely negative.\*

While this finding is in line with the idea that photo-products are not important in causing the slowing of cell division, it really does not furnish proof to that effect. The experiment was of the type that positive results would have yielded significant evidence, whereas negative results could have little meaning. The experiment just described therefore, proves only that the presence of (p) has not as yet been demonstrated. It is clear that if the egg membranes were se-ni-permeable to (p), allowing it to pass outward only, or that if (p) were changec chemically upon reaching the sea water, the experiment could not be expected to demonstrate (p). Thus, while instruc-

<sup>\*</sup>That is aside from a slight effect (1 to 2 per cent of the maximum catainable effect) that could be obtained by treating sea water abne.

tive, the finding serves mainly as a guide for further work.

In addition to comparing the response of sea urchin material with that of the photographic plate, it is of interest to compare it with another which in some respects is more like that of the sea urchin. Redfield and Bright<sup>7\*</sup> found that exposure of *Nereis limbata* eggs before fertilization to roentgen and beta rays caused an increased swelling

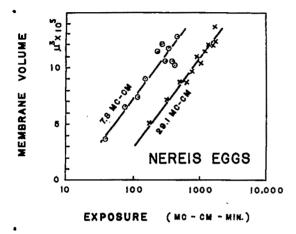


Fig. 7. Curves showing membrane volume in *Nereis* eggs after various exposures to beta rays. (Data from Redfield and Bright.)

of the fertilization membrane of the egg upon fertilization, and that the degree of swelling varied linearly with the logarithm of the dose of radiation administered (Fig. 7) for the major portion of the range of the reaction. Moreover, it was found that the reaction involved was limited to extranuclear components and that it was irreversible. The authors pointed out in connection with their observations that the findings are consistent with the view that the physiological effects of the radiations are due to the ionization of some substance in the jelly material of the egg.

Thus, in both the Arbacia and Nereis materials radiation produces latent effects which become manifest only upon fertilization; the irradiation effect is irreversible in Arbacia sperm and Nereis eggs, but not so

in Arbacia eggs; the significant change brought about appears to be produced in nuclear material in case of Arbacia and in extra-nuclear material in case of Nereis; and in both Arbacia and Nereis the effect appears to vary with the rate at which some particular protoplasmic material is used up or destroyed. It would seem, therefore, that while there are certain significant differences in some parts of the reactions, the general character of the mechanism involved may be quite similar in the two cases.

Investigation of the relation of absorbed energy and the size of certain morphological entities involved in the reaction provide further instructive information. From the definition of the roentgen, one such unit of radiation produces approximately  $2.1 \times 10^9$ ion pairs per cubic centimeter of atmospheric air (the exact number being known very closely for standard conditions). Hence, assuming that the energy absorbed by any material is nearly proportional to its density, the number of ion pairs produced by one roentgen in I cc. of water or tissue is approximately 850 times that produced in air or 1.785 × 1012 ion pairs: Taking the dose of a threshold detectable effect as being in the neighborhood of 2,500 r (Fig. 3) and the size of the average complex molecule of the nucleus as being in the neighborhood of 40,000 cu. A (Clark, p. 11),9 then one ion pair is produced for every 5.6 × 10<sup>8</sup> molecules. Likewise, taking the size of the sperm as 100 cu. mu, around 4.46 × 10<sup>7</sup> ion pairs per sperm must be produced in order to bring about any appreciable delay in cleavage.

Similarly, taking 300,000 r as being a dose which produces close to the maximum effect (Fig. 3)† and the size of the average molecule as above, one ion pair is produced for every 46.7 molecules and 5.35×10° ion pairs per sperm are produced.

† The round figure of 300,000 is taken from a region of the curve where it is becoming very flat. It is interesting in this connection to call attention to the fact (Table 1) that sixty-four minutes' exposure (approximately 500,000 r.) prevents all fertilization, and that in work unreported here, doses of 300,000 to 400,000 r were found adequate to prevent fertilization on the part of all but a few sperm in a sample.

<sup>\*</sup> And in previous papers.

These figures must be considered only approximate at best, but they do furnish some impression of the limits within which the changes must take place. It is clear, for example, that close to the maximum effect may be obtained with ionization occurring in only a small percentage of the molecules (a little over 2 per cent according to the figures), thus making it difficult to understand how any available sensitive substance could be used up to completion without as much as a one-to-one correspondence of ion pairs and sensitive molecules being reached—that is, unless some kind of multiplying mechanism is in effect. To obtain such a correspondence (on the basis of the above considerations) it would be necessary to show that around 50 times more ion pairs are produced than at present accounted for.

There are, of course, two rather uncertain factors used in the calculations—the exact size of the sensitive molecules and the precise amount of ionization produced in tissue per roentgen. It seems unlikely at this stage, however, that these could change enough as a result of future findings to account for the large discrepancy.

The developments, therefore, direct attention to three important questions: (1) whether a multiplying mechanism is not in some way effective—that is, whether a change produced in one molecule by ionization can be passed along to other molecules without the aid of further ionization; (2) whether large molecular aggregates may not be the sensitive units acted upon by the radiation to cause the effect observed; and (3) whether chemical change may be produced in a living system by radiation in significant amounts without ionization—that is, by excitation. It is hoped that future investigation will elucidate these points.

#### SUMMARY

1. Normal eggs of Arbacia punctulata were fertilized with sperm which had been exposed to various doses of hard roentgen rays and the time intervening between insemination and the first cleavage carefully deternined.

- 2. The following were found: (1) that (as observed previously) the occurrence of the first cleavage was definitely delayed by the irradiation; (2) that for relatively small doses none of the sperm failed to carry irradiation effect into the eggs; (3) that the amount of delay varied linearly with the logar thm of exposure for the greater range of the effect produced; and (4) that fertilization was prevented entirely only after doses of 300,000 r or greater had been applied.
- 3. These results show that cell division, in the sparticular case, can be retarded by irradiation produced in one-half the normal nuclear component, and that the effect is clearly cumulative in each cell treated, thus demonstrating that the reaction is characteristically different from the all-or-none "hit" or target type.
- 4. The shape of the dose-effect curve sugg-sts that the delay in cleavage varies with the rate at which some sensitive substrate is being changed or destroyed by the radiation.
- 5. Calculations, however, make it appear that the effects obtained cannot be attributed to ionization alone unless the sensative units are large molecular aggregate.

#### REFERENCES

- I. Henshaw, P. S. Studies of the effect of roentgen rays on the time of the first cleavage in some marine invertebrate eggs. I. Recovery from roentgen-ray effects in *Arbacia* eggs. Am. J. Roentgenol. & Rad. Therapy, 1932, 27, 890-398.
- 2. Henshaw, P. S., Henshaw, C. T., and Francis, D. S. The effect of roentgen rays on the time of the first cleavage in marine invertebrate eggs. II. Differential recovery and its influence when different methods of exposure are used. Radiology, 1933, 21, 533-541.
- 3. Hanshaw, P. S., and Francis, D. S. The effect of x-rays on cleavage in Arbacia eggs; evidence of nuclear control of division rate. *Biol. Bull.*, 1936, 70, 28-35.
- 4. HENSHAW, P. S. The action of x-rays on nucleated and non-nucleated egg fragments. Am. J. Sancer, 1938, 33, 258-264.

- 5. MIWA, M., YAMASHITA, H., and MORI, K. The action of ionising rays on sea-urchin. 1. The effects of roentgen, gamma and beta rays upon the unfertilized eggs and sperms Gann, 1939, 33, 1-12.
- HARDY, A. C., and PERRIN, F. H. The Principles of Optics. McGraw-Hill Book Co., New York, 1932.
- REDFIELD, A. C., and BRIGHT, E. M. The physiological action of ionizing radiations; evidence for ionization by β-radiation. Am. J. Physiol., 1924, 68, 54-61.
  - REDFIELD, A. C., and BRIGHT, E. M. The physio-

- logical action of ionizing radiations; path of α-particle. Am. J. Physiol., 1924, 68, 62-69.
- REDFIELD, A. C., and BRIGHT, E. M. The physiological action of ionizing radiations; x-rays and their secondary corpuscular radiation. Am. J. Physiol., 1924, 68, 354-367.
- Physiol., 1924, 68, 354-367.

  8. Redfield, A. C., and Bright E. M. The physiological changes produced by radium rays and ultra-violet light in the egg of Nereis. J. Physiol., 1921, 55, 61-85.
- 9. CLARK, A. J. The Mode of Action of Drugs on Cells. Williams & Wilkins Co., Baltimore, 1933.



### FURTHER STUDIES ON THE ACTION OF ROENTGEN RAYS ON THE GAMETES OF ARBACIA PUNCTULATA

## II. MODIFICATION OF THE MITOTIC TIME SCHEDULE IN THE EGGS BY EXPOSURE CF THE GAMETES TO ROENTGEN RAYS

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IN THE paper just preceding (and previously) it has been shown that irradiation of sperm or eggs (or both) of Arbacia punctulata with hard roentgen rays before fertilization causes a delay in the occurrence of •the first cleavage. It is the purpose of this report to give account of an investigation to ascertain whether the whole cleavage cycle—that is, the whole time from the moment of fertilization until the egg has divided—is slowed uniformly or whether certain parts are slowed more than others. This is important since it is desirable to know whether the slowing is associated with the sperm when it exists as a separate entity or with the more strictly mitotic behavior of the egg.

The events which occur between fertilization and the first cleavage have been carefully described by Fry. The developmental advance was noted by Fry in two ways: by observing the living material and by fixing samples at different stages which could be examined critically after sectioning and staining.

In the living egg, four stages are recognizable, due largely to various configurations of the aster and more transparent nucleus. Stage I displays a clear nuclear area having a diameter about one-tenth that of the whole egg (see photographs, Fig. I, of unfertilized eggs and eggs five minutes after fertilization). Stage 2 shows a light crescent extending almost across the whole egg when viewed from the proper angle (Fig. I, eggs fifteen minutes after fertilization). Stage 3 shows the enlarged prophase nucleus (visible in a good many of the photographs, Fig. I—see particularly the one for normal material twenty-five minutes

after fertilization). Finally, Stage 4 presents a dumbbell shaped clear area which can b∋ seen for only a short time just prior to cleavage when viewed in the right plane (visible in only a few eggs, Fig. 1). As made clear by the photographs presented here, we have noted the same stages as observed by Fr...

From a study of fixed material, Fry describes the following events as occurring:

- I. Entrance of the sperm head into the egg cytoplasm.
- 2. Elaboration of the sperm aster and movement of the sperm pronucleus toward the egg pronucleus.
- 3. Fusion of the pronuclei during whichthe identity of the sperm pronucleus becomes lost and the sperm aster becomes more prominent.
- 4. Eormation of the crescent from the sperm aster and its later disappearance.
- 5. Erophase—marked by the appearance and growth of two new asters\* and the formation of chromosomes.
- 6. Metaphase—the stage during which the chromosomes are aligned in the equatorial plate.
- 7. Anaphase—from the time when the chromosomes have separated until they begin to dissolve.
- 8. Telophase—the stage during which the chromosomes dissolve and the cell divides.

We Ikewise have observed these events and have prepared a mitotic time schedule (Fig. 5 upper part) patterned, for the most part, after the one developed by Fry.

\* These riginate close together and move to opposite poles of the egg.

Fry's observations were made on material kept at 20° C. whereas ours was kept at 25° C. While the higher temperature caused the cleavage cycle to progress more rapidly, the separate events appeared to occur at the same time with respect to each other. Thus, the figure as shown is mainly a re-

described in the previous paper, an exposure of eight minutes (62,400 r) being given. This exposure was selected because it produces a large amount of delay and would thus tend to manifest more strongly any ifferential slowing which might be produced.

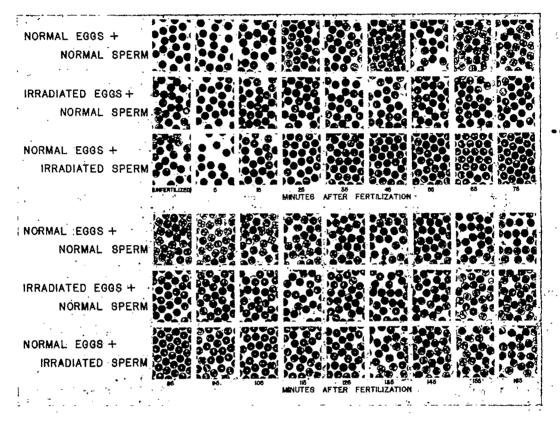


Fig. 1. Photomicrographs showing early development in *Arbacia* eggs. The first and fourth rows show normal development, the second and fifth show development after the eggs had received doses of 62,400 r of roentgen rays before fertilization, and the third and sixth show similar development after the sperm had received this dose.

production of Fry's schedule without the actual time indicated, which does not concern us particularly here.

Our problem, as stated, but which can be indicated more specifically at this point, was to ascertain whether the various stages or events occurring in the cleavage cycle maintained the same time relationship to each other although the cleavage cycle itself was much prolonged by exposure of one of the gametes to roentgen rays.

Eggs and sperm were irradiated separately in thin walled celluloid pill boxes as

After treatment three combinations of gametes were arranged:

- (1) Normal Eggs (N.E.) + Normal Sperm (N.S.) (Control Series)
- (2) Irradiated Eggs (I.E.) + Normal Sperm (N.S.)
- (3) Normal Eggs (N.E.) + Irradiated Sperm (I.S.)

The three sets of material were then watched during the course of the first cleavage cycle. After running several such series and becoming familiar with the events which can be seen in the living egg,

it was decided (1) to make photographs of the three kinds of material at ten-minute intervals beginning five minutes after fertilization, and (2) to fix samples at various stages for subsequent sectioning, staining and microscopical examination. This was done, making sure of course that the photographing and fixing did not interfere in any way with the progress of development in the eggs.

Figure 1 shows the photographic record thus obtained. In connection with this figure, it should be mentioned that about one minute was required to carry out the manipulations of making each photographic exposure. Thus, the photographs for normal eggs and normal sperm were taken one minute before the time indicated in the figure, and those for normal eggs and irradiated sperm, one minute after. This does not detract from the significance of the figure but should be taken into account.

Examining Figure 1, two points of interest are apparent pertaining to the question which has been raised.\* The first is that the marked delay in the onset of cleavage, caused by the irradiation of either gamete, is clearly manifest; and the second, that despite this, the appearance of the crescent stage is reached quite as quickly in case of the irradiated material as in case of the non-irradiated (Fig. 1, fifteen to twentyfive minutes). Thus, since in normal development, the crescent stage is reached after the fusion of the pronuclei, we may conclude that the entrance of the sperm, its movement through the egg cytoplasm, and its fusion with the egg pronucleus, are not impaired by the irradiation. Judging from Figure 1, it would seem, in fact, that this part of the cleavage cycle is speeded up, if changed at all by the irradiation. The slight enhancement indicated, however, is probably not significant because of the threeminute time interval involved in photographing the three sets of material.

The preserved material was fixed in Bouin's fluid, sectioned at a thickness of 5 mu and stained with Heidenhain's iron hematoxylir according to the well known procedure. Mass preparations were made so that the slides contained serial sections of actually hundreds of specimens. During the study of these, counts were made of the relative numbers of individuals in each sample that were in the stages listed above. The killing schedule together with the results of the counts are shown in Table 1.

Study of Table 1 yields quite the same impression one obtains by studying the slides directly. It is interesting, first of all, to no e that control material fixed three minutes after insemination shows no sperm to be present within the eggs. Investigation of this disclosed that the fertilization membrane was swept away during the course of dehycration and that since the sperm had not passed through the membrane in this lengt of time, it likewise was swept away. Since however, sperm were found within the crtoplasm when the material was fixed four minutes after insemination, it is clear that hree to four minutes are required for the sperm to pass through the membrane. Cons dering the controls farther, the figures indicate that the stages mentioned above were recognized and that these bear the relat onship to each other which is indicatec in Figure 2 (upper part).

Comparing the figures for irradiated and non-rradiated materials, it becomes clear that Stage 3 (fusion of pronuclei) is reached at very nearly the same time irrespective of whether treatment is applied to the gametes, thus verifying the conclusion above obtained by observing living material. Examining the figures farther, it will be seen that treatment of the female gametes procuces somewhat greater effects than treament of those of the male. Not only is there greater delay, but also the mitotic phases are less distinct and are more difficult to identify. Parenthetically, it should be pointed out that this finding is not congradictory to the one described previorsly2 to the effect that treatment of sperm appears to produce greater slowing than treatment of eggs. The difference is

<sup>\*</sup> Other points of interest in this chart will be dealt with in subsequent papers.

TABLE I

Stage Number												
		' i o* .	I	2	3	4	5	6	• 7·	8	8+	Total Individuals Observed
·	Minutes after fertilization when fixed								•		•√	
Controls	3 4 7 9 10 17 27 33 38 43 46	100	100 33	7 56	17 20 50	100 95 90 90 15	1 90 2	7 100 17	3 90 <b>29</b>	99		100 107 106 120 145 90 91 112 105 107
Irradiated eggs plus normal sperm	5 8 11 28 54 87 110 133 141 150		100 55	10 6ò	30 43	180 90 36		1 1 10 58 7	3	o 5 0	-	110 145 223 90 47 91 79 98 42
Normal eggs plus irradiated sperm	6 9 12 29 55 89 109 131 142		90 9	3 78 1	8 50 3	190 90 40	70 107 82	5 100	15 20. 19	15 90 85 18	5 25 82	93 95 241 93 110 112 212 115 130

<sup>\*</sup> Fertilized but without sperm in the egg cyptoplasm.

due to the fact that a lower intensity of radiation (720 r/min.) was used previously and that so much recovery occurred in the eggs during treatment with this intensity that they actually displayed less irradiation effect when measured. An abundance of data has been obtained on this point although it has not been published as yet.

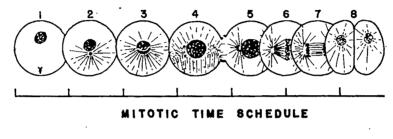
Next, an attempt was made to determine just how the time relationships of the various stages had been shifted with respect to each other. It has already been shown that Stages 1, 2 and 3 are passed through quite as quickly whether radiation is applied or not, thus leaving question only in regard to the mitotic phase of the cleavage cycle. For this, Table 1 as well as the fixed material was studied carefully with the idea of fixing the time limits of the different stages as precisely as possible. The results are shown in Figure 2.

The diagrams in the upper part of the

figure serve as an index for the graphs below. The graphs (two, upper and lower) are made up of rectangles, the width of which indicates the relative time limits of the different stages. In the upper, it will be seen that the controls—that is, normal sperm (N.S.) plus normal eggs (N.E.)—Stages 1, 2 and 3 are passed through very quickly. The limits of Stages 1, 2 and 3 and

amount of delay is not as great. Thus since Stages 1, 2 and 3 are the same in the three cases, the upper graph is in accord with what has been indicated above and in addition has the limits of certain of the mitotic phases indicated.

Now, in order to determine which stage of the mitotic part of the cycle is delayed the mest, if any, the lower graph was pre-



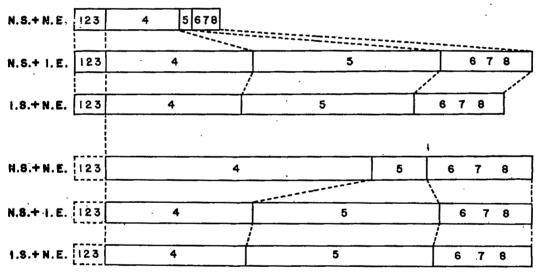


Fig. 2. At the top, diagrams showing the mitotic time schedule. Beneath, graphs showing the influence of roentgen rays on the time duration of the various stages in the cleavage cycle. See text for complete description.

6, 7 and 8 could be established sharply only in case of the controls, so that Stages 1, 2 and 3 were considered together and likewise Stages 6, 7 and 8. In case of the normal sperm (N.S.) and irradiated eggs (I.E.) it will be seen that the time between the beginning of Stage 4 and the end of Stage 8 is much greater than in case of the controls, and also that in case of irradiated sperm (I.S.) and normal eggs (N.E.) essentially the same thing is shown except that the

parec. Since Stages 1, 2 and 3 were unaffec ed by the irradiation, they are reproduced in the lower graph the same as in the apper. The linear dimension of the other parts, however, was increased in the case of the controls and irradiated sperm to have the same length as in the case of irradiated eggs, the change for each separate stage being increased in proportion to the total amount in each case. Examining the relationships, then, two things

become evident: (1) that all of the stages in the mitotic phase of the cleavage cycle are delayed by the treatment, and (2) that Stage 5, the prophase, seems definitely to be delayed more than the others.

It would seem, therefore, that as the cell enters the phase of forming chromosome bodies, it experiences the greatest injury derived from exposure of the gametes to radiation.

#### SUMMARY

1. It has been found that the exposure of sperm or eggs of *Arbacia punctulata* to large doses of radiation (62,400 r) does not

retard the entrance of the sperm into the egg, its movement through the egg cytoplasm or its fusion with the egg nucleus.

2. Further, it was found that whereas all phases of the mitotic part of the first cleavage cycle are delayed, the prophase stage was slowed to the greatest extent.

#### REFERENĆES

- FRY, H. J. Studies of the mitotic figure. V. The time schedule of mitotic changes in developing Arbacia eggs. Biol. Bull., 1936, 73, 89-99.
- 2. Henshaw, P. S., and Francis, P. The effect of x-rays on cleavage in Arbacia, a; evidence of nuclear control of division race. Biol. Bull., 1936, 73, 28-35.



### FURTHER STUDIES ON THE ACTION\*OF ROENTGEN RAYS ON THE GAMETES OF ARBACIA PUNCTULATA

### III. FIXATION OF IRRADIATION EFFECT BY FERTILIZATION IN THE EGGS

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WE HAVE shown previously\* that exposer of Arbacia punctulata eggs to roentger is causes a delay in the occurrence of the first cleavage, and further, that if an interval of time is allowed between the end of treatment and the moment of insemination, the effect is lost or reduced as a function of time—the latter being a change which has been called recovery.

While these findings were satisfactory in demonstrating that recovery takes place so far as the first cleavage is concerned, they gave no information as to whether recovery is significant for subsequent cleavages and later development or whether it continues after fertilization. It is the purpose of this report to deal with these points.

The procedure employed was as follows. Eggs and sperm were collected in the usual way from a single female and male. The collection of eggs was divided into two lots, one of which served as experimental and the other as control material. One lot was divided, placed in two small dishes and exposed to roentgen rays, one at 20 cm. and the other at 28.3 cm. distance from the target of the roentgen tube.

The roentgen-ray equipment used was the low voltage apparatus available at the Marine Biological Laboratory. The only reason for using this equipment was that no other was available at the time we wished to work. The outfit was operated at 120 kv. and 5 ma. and the intensities at the points of treatment were 720 and 360 r/min., respectively, as measured in air with a small celluloid ionization chamber, no filter being used. The duration of ex-

posurewas forty minutes, making the doses respectively 28,800 and 14,400 r.

Following treatment, each lot of treated materal was divided into eight parts and placed in Syracuse watch dishes containing 10 cc. of sea water each. Samples of each lot were then inseminated with normal sperm at the following times after the end of treatment: 0, 10, 20, 40, 60, 80, 120 and 180 m nutes. Control samples handled in precisely the same way, except for treatment, were also inseminated with normal sperm, one sample immediately at the end of the treatment period and another 180 minutes later. All samples were then allowed o develop for forty-eight hours, care being taken to keep temperature and other factors the same in each sample.

At the end of the forty-eight hour period, the organisms in all of the samples were killed with 2 per cent formaldehyde and sea water) and classified as to degree of development. For this, technique essentially the same as that employed by Mayort was used. At forty-eight hours practically all of the control organisms had developed into well formed plutei larva with arms appreciably longer than the rest of the body. This stage represented the most advanced development and was called No. 1. The irradiated material showec various degrees of development which may be listed as follows: No. 2—the two main arms equal to the rest of the body; No. 3—arms shorter than the body; No. 4—stump arms or triangular shaped gastrula; No. 5—gastrula; No. 6—blastula;

† Mavo., J. W., and De Forest D. M., The relative susceptibility to x-rays of the eggs and sperm of Arbacia. *Proc. Exper. Biol. & M*=d., 1924-1925, 22, 19-21.

<sup>\*</sup> See the papers just preceding.

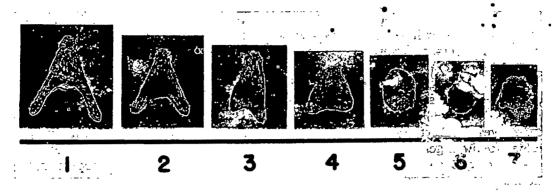


Fig. 1. Photographs showing the various degrees of development observed (see text for description).

and No. 7—no development (usually considerable disintegration). The various stages as observed are shown in Figure 1.

Classification was carried out on a quantitative basis by observing the samples under a microscope and counting the number of organisms in a given field that were in each stage. If necessary, several such fields were counted in order to make the total number of organisms observed over one hundred in each case. The values obtained were then placed on a percentage basis so that the results of different experiments could be compared.

Tabulation of the results in this manner gave the relative numbers of organisms in each sample that had reached the different stages, but we were in need of some numerical value that would represent the degree of development, or average development, of each sample in order that the advance of the different samples could be compared. Following Mavor's technique still farther, such a value was obtained by multiplying the relative number of organisms in each stage by the stage number and adding together the values thus obtained. It will be seen that by this procedure, the

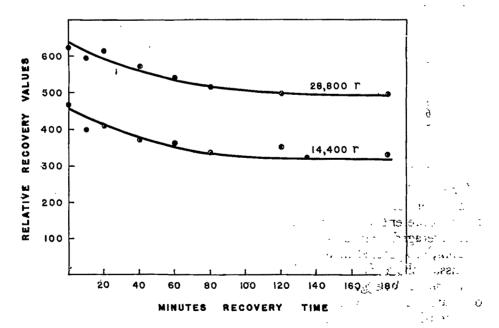


Fig. 2. Curves showing the degree of development after exposure to roentgen rays and various times allowed for recovery between the end of treatment and the moment of insemination.

greatest amount of development among the different samples will be represented by the smallest numbers, and conversely, that the largest amount of injury will be represented by largest in bers. The intervals between the stage of course, are not the same causing the values to vary among themselves; in the less, the averaged values follow the energy to allow deductions that lead to the unswer sought.

just the averaged figures in order to obtain a correct impression of what occurred and to evaluate the results properly. Consider the results for the control material. The reason for inseminating non-irradiated organisms both at 0 and 180 minutes after the end of the treatment period was to make certain that aging alone did not injure the eggs. If one considered only the averaged values, it would appear that aging impreves the developmental possibilities.

TABLE I

			1	ARLE I								
	Non-Irradiated		Irradiated									
Minutes after treatment when fertilized	0	180	0	10	20	40	60	80	120	180		
Exp. No.			28,8∞ r									
1 2 3 4 5 6 7 Av.	193 198 196 150 258 465 158	198 194 192 138 143 244 153	561 614 644 616 688 695 545	521 603 602 692 673 651 445	-56 €73 €38 €88 €69 €43 -€37	493 620 651 693 574 565 408	499 517 569 693 594 608 333 544	509 514 458 668 568 608 310	445 566 503 680 445 514 352 5∞	428 540 464 689 516 573 328		
3 4 5 6 7	193 198 196 150 258 465 158	198 194 192 138 143 244 153	332 489 510 525 527 618 286	348 422 310 504 424 549 246	三7 三7 三7 55 55 至5 至5 至6	325 325 255 588 324 565 219	302 381 329 668 390 295 201	282 336 244 654 356 333 164	295 301 259 563 326 474 242	276 298 254 606 241 481 174 .		
Av.	231	• 180	469	400	410	371	366	338	351	332		

The results for seven experiments, carried out on different collections of material and on different days, are given in Table 1. The averaged values, shown in the last column, are plotted in Figure 2 where the abscisses shown the date after treatment ended we have eggs were fertilized and the ordinates the averaged values in each case representing the degree of development.

On going over the data in Table 1, it is seen that one must consider more than

But, if one considers the individual experiments, it will be seen that the discrepancy comes largely from one experiment (Exp. 6) where some accidental injury was apparently inflicted on the control sample which was inseminated immediately at the end of the treatment period. From the other six experiments, it is clear that three hours' aging loes not alter the response of the controls in any significant way and that the values for the control samples may be com-

pared directly without correction or ada that development had proceeded further in those samples which had been allowed the

Considering the data for the irradiated material, it will be seen that the values are somewhat irregular. This may be due largely to two things: (1) that the test material was not in the optimum condition since the experiments were carried out late in the spawning season for Arbacia; and (2) because the developmental stages used did not involve the same time intervals, as mentioned above. Since, however, the variation appears to be of a heterogeneous character, the results for a number of experiments are more dependable and the averaged results indicated by the curves may be taken as the most reliable evidence of the degree of development attained after the various times allowed for recovery.

For either dosage used, it is clear that the beginning of the curves is at a higher level than at the end, that the downward trend starts at the beginning, and that the descent is more rapid near the beginning than near the end.\* It is clear, therefore,

those samples which had been allowed the most time for recovery, and that the curves bear characteristic sing rities to those based on delay in the con e of the first cleavage, furnishing with the answer we set out to obtain the recovery time following for the Tiolio compared to that before that little, if any, recovery stok place fertilization and accordingly `li\_ zation acts to stop the recover ۶, thus preserving whatever irradiaact was present at the moment police. zation. 11.97

#### SUMMARY

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On the basis of the above observations, it appears that the recovery from irradiation effect which takes place before retilization and is manifest at the place of occurrence of the first cleavage is significant in subsequent cleavage and later development; and consequently, that fortilization acts to fix whatever irradiation effect is present at the moment of fertilization.



<sup>\*</sup> The slope of the curves and the point at which they level off are not significant here for these characters are determined by the method of measurement.

### FURTHER STUDIES ON THE ACTION OF ROENTGEN RAYS ON THE GAMETES OF ARBACIA PUNCTULATA

ANGES IN RADI SENSITIVITY DURING THE FIRST CLEAVAGE TYCLE

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shown that application of hard roentgen rays to the term cells of Arbacia punctulata before fertilization causes a delay in the occurrence of the cleavage process following fertilization. It is the purpose of this reput to deal with the delay effect obtain of only by exposure before fertilization, but also at various times thereafter; in other words, to compare the radiosensitivity of the gametes with the zygote to determine the changes in radiosensitivity which occur during the first cleavage cycle.

The roentgen-ray equipment used was the dual-tube self-rectification outfit available at the Marine Biological Laboratory and the simultaneous cross-firing technique 27'cyed. The equipment was operated at 194 kv. and 25 ma., and the beam of roentgen rays was unfiltered except for the heavy glass of the roentgen tube and the bakelite windows of the tube shield (equivalent to a filter of 0.2 mm. of copper). The output intensity, as measured in air th a small celluloid ionization chamber, was 7,800 r/min. at the point of treatment -9.5 cm. from the center of each target. The exposure periods were varied for different experiments as indicated below.

Sperm are ggs were collected in the usual was from single individuals and handled with the precautions necessary for this kind of work. For each experiment carried our, material was treated as follows: "dry sperm," a concentrated egg suspension and a diluted egg suspension were

placed under the roentgen machine in separate small celluloid containers. In addition a reserve supply of diluted egg suspension was kept in a large glass container. Then, just before throwing the switch which started the exposure, the diluted egg semple under the roentgen machine and the reserve supply were inseminated. For the first experiment to be described, the exposure was for four minutes (31,200 r). At the end of treatment irradiated sperm were allowed to fertilize samples of both mormal and irradiated eggs, and likewise, mormal sperm were allowed to fertilize norma and irradiated eggs. The following combinations were thus produced:

- (I) Normal Eggs (N.E.)+Normal Sperm (N.S.) (Controls)
- (2) Normal Eggs+Irradiated Sperm
- (3) Irradiated Eggs+Normal Sperm
- (4) Iradiated Eggs+Irradiated Sperm
- (5) Irradiated Zygotes

Besides these, separate samples of zygotes from the reserve supply were given the same identical treatment at 5, 10, 15, 20, 25, 30 35, 40 and 45 minutes after insemination. All samples were then watched and the time when 50 per cent cleavage had occurred in each case was carefully determined.

A number of such experiments was carried out and the same kind of results was obtained in each case. Since a table of data would add little to what is to be said, such is being omitted and the averaged values presented in graphs. Figure I shows the results obtained for the experiment as

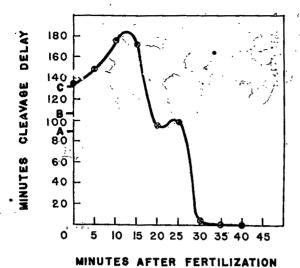


Fig. 1. Graph showing the relative radiosensitivity of irradiated eggs fertilized with normal sperm (A), normal eggs fertilized with irradiated sperm (B), irradiated eggs fertilized with irradiated sperm (C), and the zygote at various times after fertilization.

described above. The abscissae in the figure represent minutes after fertilization when 'treatment began and the ordinates the minutes' cleavage delay (i.e., over and above the cleavage time of the controls). The levels  $\mathcal{A}$ , B and C on the ordinate axis indicate the cleavage delay obtained when sperm alone, eggs alone and both are treated, respectively.

It will be seen, therefore, that for the same dose of radiation, a greater effect is obtained when eggs are treated than when sperm are treated and that the effect is still greater when both gametes are treated. These findings are thus in accord with those of the second paper of this series.

It will be seen, moreover, that the newly formed zygote and the zygote whose gametes received similar treatment just prior to fertilization have essentially the same radiosensitivity. Following this, however, the susceptibility increases for a period of ten to twelve minutes (for the conditions used) after which there is a sharp decline interrupted only by a single slight shift of some kind. The slight ripple in the descending and single slight at the descending and single slight at the descending and single slight at the descending and single slight are the descending and single slight at the descending and single slight are the descending and single slight at the descending and single slight are the descending and single slight at the slight ripple in the descending and single slight at the same radiosensity and single slight shift of some kind.

first of being due to some experimental irregularity and that if would not be manifer to in subsequent experiments. This was not the case, however, for hisplayed to some extent in every end at a carried out and when other doses of the ation were used as will be seen below. Thus, he shall be unable to attach any significance to this finding, it must report to a real response of some kind!

Figure 2 shows the curve just descending portion of the curves.

In an attempt to analyze these results, Figure 3 was prepared. Fry's mitotic time schedule, as adapted for use in the second paper, is shown diagrammatically at the

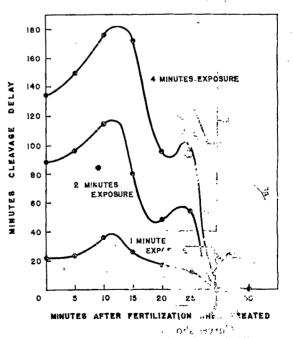


Fig. 2. Curves the same as that shown in Figure 1, but for various amounts of exposure.

top. Immediately beneath and laid out to the same time scale (i.e., the abscissae) is a reproduction of the curve from Figure 1. Below as showing changes in viscosity, allity and oxygen uptake as describe Heilbrunn, Fry and Parks, Whitaker.

fr. Figure 3, it will be noted that the fire d main peak of susceptibility to re on is reached shortly after the proave come together and that the peak is reached during the early property se stage. Moreover, it will be seen the main peak in susceptibility is reached at very nearly the same time as peaks in viscosity and permeability and that there appears to be no significant relationship between radiosensitivity and rate of oxygen uptake.

om the results (Fig. 3) one might be inc. ned to attribute significance to the fact that the three upper curves show a peak at about the same time. However, before doing so, the following must be

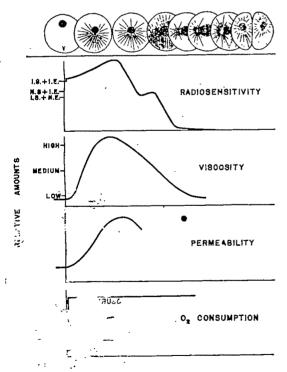


Fig. 3. Conves showing changes in radiosensitivity, viscosity, permeability and oxygen consumption at versus times during the first cleavage cycle.

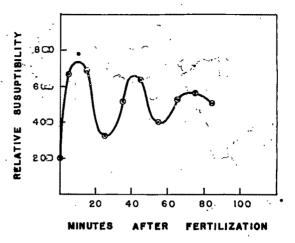


Fig. 4- Curve showing the changes in radiosensitivit; which occur in the developing egg and made evident by measurements forty-eight hours after-fertilization.

taken into account. It is clear from what has been said that the increase in radiosensitzvity takes place only during the perioc before the fusion of the pronuclei. Thus, in view of the fact that recovery occurs in the egg before fertilization and is apparently stopped by fertilization (as shown in the third paper), it is possible that recovery continues in the egg pronucleus until it fuses with the sperm pronucleus. Should this be the case, it is obvious hat as the time for recovery between the end of treatment and the fusion of the pronu-lei becomes shorter, the effect for a given dose of radiation would be found to be greater, just as was the case. Furthermore, the more rapid ascent of the curves (Fig. =) for the larger dosages is in accord with what would be expected if the increase in susceptibility were due to recovery. While there is not as yet any positive proof that the increase in susceptibility can be accounted for on the basis of recovery, this possibility cannot be excluded at this time.

Mistakes might also be made in attributing too great significance to the descent of the radiosensitivity curves, for as the actual cleavage is approached, there is less and less opportunity for the effect to become manifest should its manifestation in any way be latent. There are, however, two

points which make us believe that the descent is not due to lack of time for expression. The strict is tent appearance of the strict is the strict is tent appearance of the strict is the strict is tent appearance of the strict is the strict i the descending portion of the curves. since it does ppear determine the changes in radi so consistently, towoold seem that the course of the curves here must be determined by something other than the method of measurement. The second point has to do wit. sults obtained in another experiment

In an attempt to obtain further information on the changes in radiosensitivity which occur during development, treatments were given at ten minute intervals during the first several cleavages and the degree of development noted after fortyeight hours, using the technique described in the report just preceding. Somewhat lower doses of radiation (3,600 r) were given in this case, however, since the organisms fail to survive to the later stages when the larger doses are administered. Moreover, softer radiation was used (140 kv., no filter), but this was only because no other was available at the time the experiments were carried out.

The results obtained are shown in Figure 4. It will be seen, as before, that although the effect is measured at a much later time in development, an increase in radiosensitivity is manifest during the first ten to fifteen minutes and that this is followed by a marked decrease. It would seem, therefore, that the decline of the curves (Figs. 1 and 2) cannot be attributed to the method of measurement and that it has to do with changes going on within the organism.

Parenthetically, Figure 4, in addition, shows certain other points not heretofore noted. Following the fall in radiosensitivity during the prophase, there is again an increase which reaches a peak at or just before the actual cleavage of the zygote. There appear, in fact, to be waves of susceptibility with peaks being reached at or near the times of the first and second cleavage. These, however, have little bearing on the point in question.

#### SUMMARY

Experiments have been carried out .. to compare the radiosensic rity of gametes and pygotes of Arbacia pun a and to isitivity which occur during the asset

- 2. It was found (1) that the more susceptible than sperm when in in a tensity of  $7.8\infty$  r/min. is used; (2) equal doses of radiation, the e tained by irradiating the zygote is than that obtained by treating eit. ete alone; (3) that about the same contains obtained when both of the games, re given the same treatment as the  $z_i$  te and (4) that by two different method, measuring the irradiation effect, gotes were found to increase in same. bility until about the time the pronuclei fused and that they decreased in susc ibility during the prophase stage.
- 3. It was shown that the peak in usceptibility is reached at or about the same time as the peaks of viscosity and permeability are reached and that there is appa. ently no correlation between changes in radiosensitivity and rate of oxygen uptake.
- 4. It was pointed out that since the radiation effect is apparently produced in the nuclei and since recovery occurs in the egg only and then only until fertilization, the increase in susceptibility before fur on of the pronuclei may be due to recovery continuing in the egg pronucleus until the time of fusion.

#### REFERENCES

- I. HEILBRUNN, E. V. The viscosity of toplast Quart. Rev. Biol., 1927, 2, 230-244,
- 2. FRY, H. J., and PARKS, M. E. Studies mitotic figure. IV. Mitotic changes : cosity changes in the eggs of Arbacia, Cu and Nereis. Protoplasma, 19391121, 473-499.
- 3. LILLIE, R. S. Increase of permea dity water in fertilized sea-urchin eggs and to of cyanide and anesthetics upon this charter. Am.
- J. Physiol., 1918, 45, 406-430. 4. WHITAKER, D. M. On the rate of c sumption by fertilized and unfertil. 1 eggs. ... Comparisons and interpretation. J. Gen. Physiol., 1532-1933, 16, 497-528.

#### THER STUDIES ON THE ACTION OF ROENTGEN ON THE GAMETES OF AREACIA FUNCTULATA

INFLUENCE OF LOW TEMPERATURED TO OVERY FROM ROENTGENERY EFFECTS IN THE EGGS

By P. S. HENSHAW, 2H.D.

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BETEESDA, MARYLAND

The of the eggs of Arbacia punctulata is gen rays causes a delay in the occurrence of the first cleavage, and further, the effect will become reduced or lost the effect will become reduced or lost ess which has been called recovery.\*

An attempt to shed more light on the nature of this reaction, an experiment has been carried out to determine whether the recovery process is affected by lowering to a rature.

3 been shown previously that ex-

No. 6

te: Erature. The procedure used was as follows: Eggs were treated in the manner described previously, enough radiation being given to produce an appreciable amount of cleavage d lay. At the end of treatment, the eggs were divided into two lots, one of which was maintained at room temperature (24°C.) and the other which was placed in a tubular gless container and submerged in a beaker of water and chipped ice (o°C.). Nonirra and controls were also kept under the same ronditions at 24 and o°C. At 0,† 60, 120 a 180 minutes after the end of treatment cumples of the irradiated and non-iri- liated materials kept at the differthe tures were fertilized at mom etermined also at room temperature.

etermined also at room temperature.

series of seven different experiments
was performed, all of which showed the
same one at effect. Since the procedure
was exactly parallel in all of these,
data a typical experiment only will be
pressed a Such is shown in Figure 1.

It will be noted first of all that keeping

a sample of non-irradiated controls at o°C. for a period of three hours did not after the cleavage time and likewise that aging in this particular case did not after the cleavage time. It is safe, therefore, to compare the experimental samples directly.

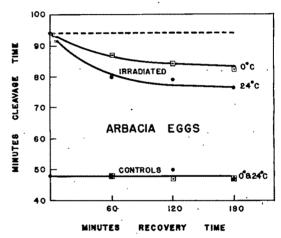


Fig.1. Curves showing the effects of temperature on re-overy from roentgen-ray effects in *Arbacia* eggs.

The curve for material kept at 24°C. is typica of a great many we have obtained by this procedure. It drops away rapidly at firs but tends to become parallel with the base line. It is obvious that if the lower temperature prevented any recovery from taking place, the experimental points so obtained would have fallen along the dotted line at the top of the figure. Similarly, it is evident that if it did not influence the recovery process in any way, the points would have fallen along the curve obtained for room temperature. As, in. le evident by the figure, they did not fail-in either of these places but intermediate. It is clear,

<sup>\*</sup> See the third paper of this series.

<sup>†</sup> The immediately at the end of treatment.

therefore, that temperature does have an femperature would permit cons

effect on the recovery process, lower temperature tending to the perature tending to the perature tending to the prest, knowing the from 24 to o°C. reduce just hor the face or covery varies with of recovery observed.

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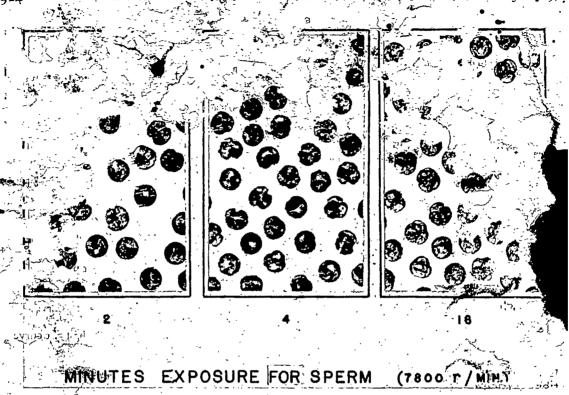


Fig. 1. Photomicrographs arranged to show that the proportion of organisms manifesting multipolar cleavege varies with dose of radiation administered.

ments have been carried out. The various points will be taken up in much the same order as investigated.

#### - - POLYSPERMY

In view of the fact that polyspermy is known to produce multipolar cleavage (Beyeri, and others) and that radiation applied to gametes has been said to induce polyspermy (Packard¹o), it was suspected that this condition might be responsible for the multipolar cleavage observed in the self-in material. To investigate this point, serial sections of eggs fixed when the two pronucleis are clearly visible were examined for the presence of extra sperm pronuclei. In fact, complete series of serial actions of more than or hundred areated individuals and store than one hundred areated duals were examined.

Positive rach ion of pro-

be done with reasonable certainty if good preparations are available and preper precautions taken. In the material in qualce, the sperm pronucleus is accompanied by a sperm aster which is rendered const uous by Heidenhain's iron hematoxylin stain. This was always used as the final distinguishing feature in identifying the sperm pronucleus.

of the 100 control specific as examined, all except two were found to single sperm producteus and the sperm producteus and the sperm producteus and the specimens revealed about the same size tion. In this case also, all enter sperm found to contain a single sperm producted and one since ot samples of the material did ayed a high permultipolar condition as observed here was at can not due to polysper.

# FURTHER STUDIES ON THE ACTION OF ROENTGEN

VI. PUODUCTION OF MULTIF LAR CLEAVAGE THE EGGS BY EXPOSURE OF THE GAMETE TO ROEN 1550 PRATS

By P. S. Z.ENSHAW, Ph.D.

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BETHESDA, MARYLAND

IE preceding reports attention has called to the production of one har effect in Arbacia punctulata eggs by exposure of the gametes to make a punctulata eggs. In the present infirst cleavage. In the present infirst cleavage. In the present infirst of development, particularly tipolar cleavage.

It was observed in connection with the well described in Papers I, II and IV of this group, that, in addition to delay in the first cleavage being caused by irradiation, cleavage is often abnormal in that more than two blastomeres were formed. This is made especially evident in the chart, Figure I, Paper II. Referring to this chart, it will be seen that when cleavage finally occurs in those specimens receiving radiation, a large proportion of the divisions are multipolar in character, and further, that this is the case irrespective of whether the radiation is applied to the sperm or the eggs.

That multipolar cell division may be produced by exposure of cells to high energy radiation has been mentioned by several investigators (Hertwig, O.; Hertwig, O.; Packard; Politzer, 1934; Sonnenblick, Politzer, 1934; Sonnenblick, le some importance has been attached to the observation, the information available has not been sufficient to allow really significant deductions. In the present as the effect has been obtained with such use that a variety of experiments has a carried out and considerable innation obtained. Among other things, we shall accuss what appears to be an important mechanism of cell death and how

irradiation may, by the same mechanism of action, produce either death or malignancy.

SPECIAL CONSIDERATIONTS

At the outset it is interesting that both delay and multipolarity should be caused, by the same treatment, for it is clear that the two mechanisms of response are governed by quite different principles. Cleavage delay is a cumulative process in each cell, a fact which is made especially clear in Figure 1 of the first paper. Except for extremely low doses, some effect is manifest in every cell and the amount of effect displayed by each cell increases as the amount of radiation applied is increased. Multipolar cleavage, on the other hand, is an . all-or-none process—either the abnormality occurs or it does not. Aside from the number of cells formed at the time of cleavage (cf. below), it is evident that various degrees of this effect cannot be observed in the organisms and that increasing the dose of radiation could manifest a greater effect only by producing the abnormality in a greater proportion of the organisms in a sample receiving treatment. Parenthetically, it seems that two better examples. could not be obtained to illustrate the characteristic differences between the cumulative and the all-or-none types of response.

Although the two effects are manifest at the same time in the same organisms and caused by the same radiation treatment, question arises as to whether there is really a close relationship between the two responses. To investign a this and the significance of multipolar cleavage, extensive use has been made of the fixed material described in Paper II and certain experi-

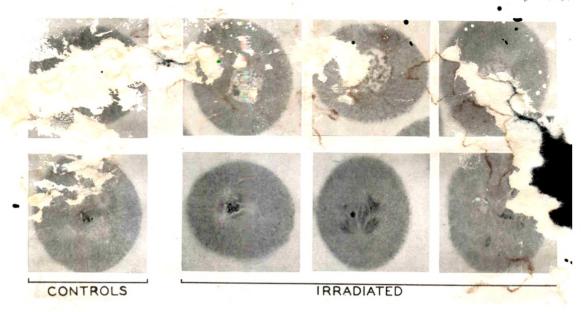
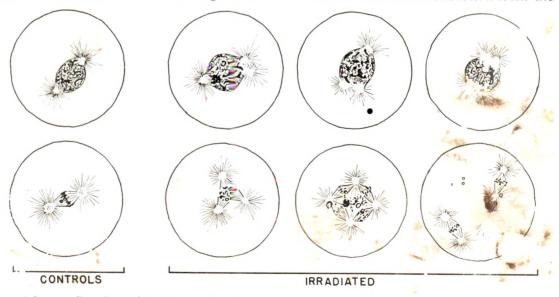


Fig. 4. Photomicrographs showing the mitotic configurations of zygotes whose sperm had received no radiation (controls) and whose sperm had received 62,400 r (irradiated).

In view of the fact that sperm contain almost no cytoplasmic material, it would seem that cytoplasmic changes are not responsible. Further, in view of the fact that the egg contributes no aster as does the sperm, it would seem that irradiation of this body is not responsible. The latter point is strengthened by the fact that the sperm aster apparently completely disappears following the crescent stage and is

replaced by two new ones that are functional in mitosis. Consideration of these various points leads to the presumption that a change produced in the nucleum aterial (even a single gamete) by the irradiation, in some way induces the formation of accessory asters and that these in turn cause the chromatin to be divided several ways.

This is a reasonable deduction from the



rig. 5. Drawings of the figures (Fig. 4) as supplemented by adjacent sections in each case.

duced by radiation does vary with dosage and hat the reaction is of the multiple action type.

NES.S AND ANDROGENESIS (1914) has stated that in the reis material, irradiated sperm stimulate the egg without being h into it. (2) stimulate and be drawn t fusing with the egg nucleus, and date, be drawn in and fuse with egg leus, but interfere with develop-Development in the first two cases. ore, is by gynogenesis. Packard states ther that androgenesis may likewise be roduced in this form by properly exposing tre eggs. Other investigators (Hertwig, O.,4 ng irog material; Hertwig, G., using trog and sea urchin; Oppermann,8 using trout; Dalcq, using frog; and Simon, 11 using frog) have likewise stated that certain large doses of radiation applied to either gamete will allow fertilization but nevertheless prevent the irradiated pronucleus from participating in subsequent mitotic activity. In Paper II we have stated plainly that in the sea urchin material, as used by us, fusion of the pronuclei takes r'ace quite as rapidly when one or the other gamete is heavily irradiated as when neither is irradiated. The evidence supporting this conclusion is based upon obser rations of living specimens and cytological examination of fixed material. In connection with the present consideration, we wish to indicate just how definite the cytological evidence is on this point and consider the re sible meaning.

as any peen heavily irradiated (62,400 r ap) one of the gametes). Such reference would seem permissible in view of the fact that 50 or will produce a threshold remember them and since 5,000 to 10,000 r is tolerance limit for a human patient even the divided dose treatment is a dispread over a long period of time. Thus, while our cytological observations do to pertain to material receiving a variety of doses, some evidence of nonfusability of

the producted should have been made if this were an important according to sent of the sen

#### FIRST EVIDENCE OF MULTIPOLARITY

Since the multipolar cleavage enserved could not be accounted for or the series of polyspermy, differential slowing of the divisional rhythm of the nucleus and to plasm, or a tendency for the pronuclei to remain apart, it was decided to reverse the procedure and look for the firs' evidence of multipolar cleavage. Thus, we began with samples which showed outstanding displays of multipolar mitotic figures, and proceeded progressively back over those fixed at earlier periods in the mitotic cycle. The results of our findings are indicated in Figures 4 and 5. The lower rows show the types of mitotic figures which may be found, whereas the upper rows show the stage just previous. The stage preceding this is the one shown at the bottom of Figure 3, which, as indicated, is the same irrespective of whether radiation has been applied. It thus becomes evident that the multipolar condition, at least in some cases, begins with the appearance of supernumerary asters. Whether these arise de novo or from preëxisting asters is not yet apparent, but it seems abundantly clear that because of them, chromatin material predetermined under normal conditions for two blastomeres is distributed among more than two and sometimes several.

This raises the very interesting question of what initiates the formation of asters. In the present case, accessory ones are produced by irradiation of either gamete.

a fairly extensive literature indicating that they tend to remain apart under certain conditions. The matter might be disped on the grounds that other radiations and other kinds of test material were used in the previous cases, except for the fact that G. Lertwig<sup>5</sup> also used a species of sea urchin (Parenchinus miliaris). Thus, it

treated sperm now enter the egg, stimulate it to development, but not participate in its subsequent missing activity. Figure 6 is a reproduction of the ind of evidence he found.

nuclei occurs rather cor if not entirely so, even in as into.

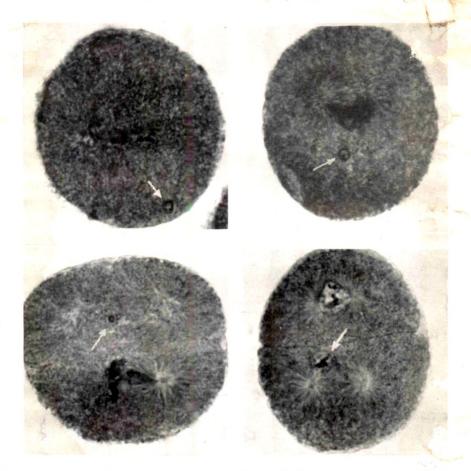


Fig. 7. Photomicrographs of *Arbacia punctulata* material displaying a body which has all pearances of being the same as the extra-nuclear one believed by Hertwig to be irradiated sperm p. material

would perhaps be well to cite the evidence for lack of fusion of pronuclei as presented by Hertwig.

After observing that the degree of abnormality increases with exposure up to a certain point beyond which it decreases again in certain forms, Hertwig set out to discover whether cytological evidence could be obtained in sea urchin material to confirm the hypothesis that heavily

however, the late prophase stage vist ys a small body of deeply a ning materiallying free in the evrope. Hertwig was led to believe to this in the diated sperm pronuclear material and the parameters of active nucleus—indeed a reasonable tion from the morphological characteristics displayed. With this in mind, similar stages of our material were examined for the

tri- and quadripolar mitotic figures (Figs. mind, our material was reexamined to re 4 and 5), for in these cases, it would whether any appreciable number of ch that the homogerous chromat figures apt simply dr me to more than pros, whethere 1: but this scheme would not seem to suggesting incomplete " ... my in case of the lower rightcould be found. Briefing a (20 per cent or more) of the m where the mitotic configuration dra in

Fig. 6. Reproduction of Hertwig's figures showing evidence of sperm pronuclear material which did not enter into fusion with the egg pronucleus. Note that the identity of the sperm material becomes almost, if not complictely, lost.

good bit more elaborate. It is difficult to inderstand how the chromatin in this case could have become so distributed if at the stage just previous it was localized in a geneous mass. The elaborate ight be expected to result more hat the from a condition in which the chromatin material is rather widely scattered at the stage just prior to the formation of spindles—as, for example, the incomplete fusion of pronuclei. With this in

were of the elaborate type and still no cytological evidence of incomplete fusion could be found—that is, aside from that which is to be given immediately below, but which in the end seems to confirm this conclusion.

Strong evidence has been presented in Paper II and again above indicating that for a large dose of radiation applied to either gamete, the pronuclei fuse definitely and without question; yet we have quoted

to cause the chromatin ordinarily intended for two cells to be distributed among more than two, thus rausing a har ge chromatin in the cell most cases cell death. The loss of the matin in irradiated cells due to other means\* has been extensively described in the literature, but little attention has been given to loss due to multipolar cleavage especially when accessory, astral systems appear to be the inciting agents. In emphasizing this, we recognize the fact that accessory asters have been induced in cells by a variety of agents with the consequent multipolar cleavage and cell death. However, it is nonetheless significant that irradiation may cause cell death by this procedure.

Recognizing that chromatin may become abnormally distributed in cells after exposure to radiation and taking into account one of the significant theories of cancer, we are able to indicate how radiation by the same mechanism of action may act in the well known dual capacity to produce death in cells on the one hand and malignant growth on the other. Boveri, a good many years ago (see the 1929 translation), set forth what remains today as one of the most plausible theories of cancer. Basing his theory on observations of multipolar cleavage in sea urchin eggs by polyspermy, Boveri pointed out that loss of precisely the right chromosome component might be expected to unleash certain malignant behavior on the part of the daughter cells.

While, in the light of more recent genetic development, it is clear that far reaching biological changes (including cell death and perhaps malignancy) may result from modifications involving much less than whole chromosomes, the modern conception of the cancer problem attests the feasibility of the broader aspects of the Boveri Theory. In a recent U. S. Public Health Report (Reprint No. 2008) is a paper prepared by a committee of prominent investigators† appointed by the

Surgeon General to "formulate,/as far as could be done, the fundamental aspects of he cancer problem." In this report the ollowing statement api ars: "The new property (malignert), arg uppears to develop surdenly. 1 are Ad charac-'~endants. ter, and is transmitted. It gives evidence of 1 tation."

Jssibly " wit Thus, since cancer m from mutation, since mut tion r duced by abnormal distribution ? tin and since cells usually die a of such distribution, it seems of ar & at radiation may by the same mes anism action act in the dual (seemingly paradoxic cal) capacity to produce either death or malignant growth.

#### SUMMARY

1. It has been observed that application of high energy radiation to either gamete of Arbacia punctulata just prior to fertilization will, in addition to causing delay in the onset of cleavage, also cause the cleavage to be multipolar; in fact, close to 100 per cent of the individuals in a sample will be found to manifest this effect if the dose administered has been adequate.

2. The reaction has a definite threshold dose and goes to completion in a fairly

narrow range of dosage.

3. Although several possibilities were investigated, there is no evidence that delay in cleavage and multipolar cleavage are dependent on the same charge produced in the cells by the irradiation.

4. The multipolar condition is not due

to polyspermy.

5. The cytokinetic and karyokinetic rhythms are not thrown out of p. se with

respect to each other.

- 6. For doses of radiation that will produce close to 100 per cent multipolar cleavage in the samples of material, they is no evidence on incomplete fusion nuclei.
- the عدام 7. The first signs of multipe ... appearance of accessory asters. These ap-

<sup>\*</sup>Such as fragmentation and failure of whole or parts of chromosomes to go on the equatorial plate properly during

<sup>†</sup> Consisting of Stanhope Bayne-Jones, Ross G. Harrison, C. C. Little, John Northrop and James B. Murphy.

presence of such bodies. Figure 7 shows the kind of thing we were able to find in a good many instances. It is thus clear that our material contained bodies having appearances single finot precisely the same as those the contained by Hertwig.

3

2

Grand this body might well be isolated its property of the share of the state of th statefial, as believed, it seems that 2 of its independent existence stand all the way back to the pronuclei stages. In our case, however, the et aence of such continuity was even less than Hertwig's which indeed was scant enough. In our material, the late prophase nuclei displayed no heavily staining bodies as did Hertwig's. Almost without exception, the early prophase stages were as free of any such object as indicated by the photomicrographs in the top row of Figure 4. It seems to us, therefore, that the extranuclear body of the late mitotic stages must arise de novo. Just where it first apn rs is not clear, but it seems improbable that it can represent exclusively sperm pronuclear material which is aborted off by -the late prophase nucleus. As concrete evidence that this body is not irradiated sperm pronuclear material, we may state that it can also be found when nonirradiated sperm are used and in the case of irradiated eggs.

Thus, after considerable apprehension, it seems at we may safely and finally conclude wat for the conditions used, the pronucti fused to the extent that the individus wents could not be distin-Ashem : Et our investigations have not wered chiological evidence as to whether higher doses of radiation would tend to ause the principle to remain apart; but, in this connection, it is to be emphasized the description (2,400 r) was adequited to the maximum dela and nearly 100 per cent leavage, thus making the possi-"-mulling" bility of incomplete fusion for higher doses seem unlikely. While there is some difference between Hertwig's findings and ours, it seems to be more a matter of interpretation than observation. Hertwig's strongest evidence of incomplete fusion is based on the fact that the cleavage cells appear to have more nearly the haploid rather than the diploid number of chromosomes. Considering the confusion that may arise in connection with this kind of evidence; it seems not quite adequate to settle the question completely. In any case, the finding of the extra-nuclear bodies in the late mitotic stages of control and irradiated egg materials surely takes precedence over this evidence.

While we have indicated that as long as the irradiated sperm is able to penetrate the egg, it will fuse with the egg nucleus in case of Arbacia punctulata, we do not wish to imply that such may be the case generally. Packard's work with Nereis material and that of others with Amphibia material (including unpublished work of our own) are so abundantly clear, indicating that pronuclei may be caused to remain apart by irradiating gametes, there seems little doubt about it. We therefore take the position that the behavior of pronuclei of different forms may vary in this respect.

#### DISCUSSION

Having thus disposed of the question of the fusion of pronuclei, and with the assurance that for doses capable of producing close to 100 per cent multipolar cleavage there is fusion to the extent that the separate elements cannot be distinguished, we wish to return to the matter of multipolar cleavage and indicate what appears to be an important mechanism of cell death.

It is a recognized biological fact that the loss of chromatin usually results in serious injury to a cell and most often in cell death. Hence, shortage of chromatin in cells resulting from multipolar cleavage (or any other type of action) may be expected to be injurious or lethal. From what has been said, it appears that irradiation in certain cases may act on nuclear material in such a way as to cause accessory asters to form and that these in turn act during mitosis

parently act to cause the chromatin ordinarily predestined for two cells to be divided among several, thus causing chromatin deficiencing in the cell progeny.

8. By r ass of l'imination, it appears that as a result as produced in the nuclear as a result as a re

9. It ing fact, although no significance has sen attached to it as yet, the multivolar condition may be indiation of half a normal nucleus is, a gamete.

death, it has been pointed out that probably one of the important mechanisms by which irradiation causes cell death is the production of accessory asters, which in turn cause the chromatin to be abnormally distributed at the time of mitosis.

11. Further, in view of the fact that chromatin modification stands as one of the plausible explanations of cancer, we are able to point out how radiation may, by the same mechanism of action, function in the well known dual capacity to produce cell death on the one hand and malignancy on the other.

#### REFERENCES

- 1. Boveri, T. Ueber mehrpoligie Mitosen als mittel zur Analyse der Zellkerus. Verhandl. d. phys.med. Gesellsch. zu Würzb., 1902, 35.
- 2. BOVERI, I. The Origin of Malignant Tumors. Tr slated by Marcella Boveri. Williams & Wilkins Co., Baltimore, 1929.
- 3. Dalco, A. Interprétation cytologique des effets,

sur la gastrulation, de l'irradiation d'un des gamètes, chez Rana fusca. Compt. rend. Soc.

- 4. Hei Jao, 104, 1255-1058.

  4. Hei Jadiumkrankheit tierischer Ke. azelt Franzischer Zeugungs- und Vererbungslehre. Arch. f. mikr. Anat., 1251, 77, 1-35; 97-164.
- mikr. Anat., 10<sup>-11</sup>, 77, 1-35; 97-164.
  5. Hertwio, G. Dos, Schicksal des mit Radium bestrahlten Spermachromatins im Seeigelei.
  Arch. f. mikr. Anat., 1912, 79, 201-241.
- 6. Lea, D. E., Haines, R. B., and Coulson, C. A. The mechanism of bactericidal action of radioactive radiations. *Proc. Roy. Soc. Lond.*, s.B., 1936, 120, 47–76.
- LORENZ, K. P., and HENSHAW, P. S. Action of 200 kv. x-rays on Achromobacter fischeri. In press.
- 8. OPPERMANN, K. Die Entwicklung von Forelleneiern nach Befruchtung mit radiumbestrahlten Samenfäden. II. Das Verhalten des Radiumchromatins während der ersten Teilungsstadien. Arch. f. mikr. Anat., 1913, 83, 307–323.
- PACKARD, C. Effect of radium radiations on development of Chaetopterus. Biol. Bull., 1918, 35, 50-71.
- IO. PACKARD, C. Effect of radium radiations on fertilization of Nereis. J. Exper. Zool., 1914, 16, 85-129.
- II. Simon, S. Effets de l'irradiation d'un des gamètes sur la gastrulation, chez Rana fusca. Compt. rend. Soc. de biol., 1930, 104, 1052-1055.
- 12. STRANGEWAYS, T. S. P., and HOPWOOD, F. L. Effects of x-rays upon mitotic cell division in tissue culture in vitro. Proc. Roy. Soc. Lond., s.B., 1926, 100, 283-293.
- 13. Sonnenblick, B. P. X-radiation of the mature gametes of Drosophila melanogaster; cytologic abnormalities and egg mortality. *Genetics*, 1938, 23, 169.
- 14. U. S. Public Health Report. Fundamental Cancer Research. Vol. 53, 2121-2130. Reprint 2008.



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#### E D I'T ORI



THOMAS ALLEN GROOVER 1877-1940

and Sarah Jane (Joiner) Groover. His father, who was a farmer, was a Confederate soldier during the Civil War and had lost

an arm in action. Dr. Groover received his early education in the public schools of Brooks County, Georgia. Bec cial considerations it did not for him to continue his econom, but through the good offices of the Hon. Hoke Smith of Georgia, who was Secretary of the Interior in President Cleveland's Cabinet. he was appointed as assistant messenger in the Department of the Interior. He then came to Washington in 1893 and resided there all the remainder of his life. In 1894 he entered the Medical Department of Columbia University, which later became The George Washington University, and graduated therefrom in 1898. In 1926 his alma mater conferred upon him the degree of Doctor of Science. After internship at the Garfield Memorial Hospital he was appointed physician with the Isthmian Canal Commission and in that capacity spent the next year in Nicaragua.

Dr. Groover returned to Washington in 1900 and entered the general practice of medicine. At the same time he began work in roentgenology at the Central Dispensary and Emergency Hospital. Although he did not completely specialize in radiology until 1912, he was actively engaged in that field from his entry into it in 1900 up to within three months of his death which occurred on April 20, 1940. It was in those early days from 1900 to about 1904 or 1905 that he suffered the injuries to his hands which resulted in amputation through the left forearm in 1926 and in final involvement of the right axilla and lung which cost him his life.

Dr. Groover was closely associated with the scientific progress and the organizational development of radiology in this country during the entire first forty years of the present century. He made numerous contributions to the literature and was always interested and quietly helpful in everything that affected the welfare of the specialty that he loved. He was insistent, however, that the radiologist is primarily a physician, and as such he always established a personal relationship with every patient who came under his care. His mem-

bership in medical organizations included the following: Medical Society of the District of Columbia. of which he was President in 1925; Fellow of the merican Med-Fellow the American ical Association College of Physicians mber of the Southern Medical Associa of which he was Vice-President in 192 member of the American Roentgen Ray Society, and its President in 1925; member of the Radiological Society of North America: Fellow of the American College of Radiology in which he served both as President and as Chancellor.

Dr. Groover's work as a practicing radiologist was characterized by the utmost painstaking care and attention to detail. He not only required the best possible technical work but spared no time nor personal effort to arrive at a correct interpretation and final diagnosis. He had developed in himself to a very high degree those qualities which are indispensable in the good physician, accuracy in observation and a keen sense of relative values. He was a diagnostician of unusual ability. In manner Dr. Groover was quiet and reserved. Being of a very studious habit, he made it a rule to spend at least one hour a day in the reading of medical literature. He had great qualities both of mind and heart which were unusual and outstanding. His ab v as an organizer and executive wa known. His careful, methodical att to all the details of bookkeepir cords and management laid the for his professional work. He al ... ys looked upon business arrangements, however, as a means to more important end ras st and last a physician. Even every branch of which he was pr insisted must always be looked upon as an integral part of general m dicar practi were patience and a gree car methodical, painstaking care in ever nostic and therapeutic proc e. H 10minant moral characteristic v Jake not se . of justice, right and fair dealing. He had an unfailing patience in compromising differences of opinion among his associates, a sane judgment in arriving at important decisions, and above all, a kindly, tolerant charity towall with wom he could not agree. He will be greatly massed by his close associates who we customed to call upon him almost to rhis helpful coun-

sel, and his loss will be keenly felt in many organizations in which his advice was highly . His death adds another martyr to coll of those who have sacrificed them are in the interests of science and humanity.

ARTHUR C. CHRISTIE





# SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

#### MEETING . ROENTGEN SOCIETIES\*

UNITED STATES OF AMELICA AMERICAN ROENTGEN RAY SOCIETY Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Hotel Statler,

Boston, Mass., Oct. 1-4, 1940.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Next Annual Meeting: Commodore Hotel, New York City, June 12, 1940. Section on Radiology, American Medical Association

Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: New York City, June 10–14,

RADIOLOGICAL SOCIETY OF NORTH AMERICA

Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Cleveland, Ohio, Dec. 2-6,

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY Secretary, Dr. Walter L. Kilby, Baltimore. Meets third

Tuesday each month, September to May.
RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY

Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September. Section on Radiology, Illinois State Medical Society Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill. Next meeting, Peoria, Ill., May 21–23, 1940. Radiological Section, Los Angeles Co. Med. Soc. Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building. month at County Society Building

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY Secretary, Dr. L. J. Taormina, 1093 Gates Ave., Brooklyn, N. Y. Meets monthly on first Tuesday, October to · April.

BUFFALO RADIOLOGICAL SOCIETY

Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY

Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to May inclusive at the Hotel Sherman.

CINCINNATI RADIOLOGICAL SOCIETY

Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to .May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY

Secretary, Dr. H. A. Mahrer, 10515 Carnegie Ave. Meets t 6:30 P.M. at Mid-Day Club rooms on fourth Monday month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB

Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

Deragit Roentgen RAY and RADIUM SOCIETY cretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY

Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meerings in May and November.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical .. secont .cn of Georgia in the spring.

Secretary, Dr. Wint Delloilander, St. John's Hospital, Springfield, ill. Meetings held quarterly, on the fourth Sanday of the monin. INDIANA ROENTGEN SOCIETY

Secretary, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis,

Ind. Meeting beld the second Sunday in May annually.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. J. C. Bell, 402 Heyburn Bldg., Louisville.
Meets annually in Louisville on third Sunday afternoon in April.

Long Island RA SLOGIC L SOCIETY

Secretary, Dr. acus Viener, 1430-48th St., woklyn, N. Y. Meets Kings County M. G. Soc. Bldg. centhly on fourth Thursday, October to May 8:20

MICHIGAN ASSOCIATION OF ROENTC GIS Secretary, Dr. J. E. Lofstrom, 1530 J.Wi. g., Detroit. Three meetings a year, Fail, Wi. t. . . rg.

MILWAUKEE ROENTGEN KAY SOCIETY Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital. Milwaukee, Wis. Meets monthly on first Enlay at Milwaukee,

versity Club. MINNESOTA RADIOLOGICAL SOCIETY

Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

NEBRASKA RADIOLOGICAL SOCIETY

Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY

Secretary, Dr. W. J. Marquis, 198 Clinton Ave., Newark. Meets annually at time and place of State Medical Seciety. Mid-year meetings at place chosen by president.

NEW YORK ROENTGEN SOCIETY Secretary, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY Secretary, Dr. Major Fleming, Rocky Mor nual meeting at time and place of State Medica. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year-January, May, November.

PACIFIC ROENTGEN CLUB

Secretary, Dr. L. H. Garland, 450 Sutter St, cisco, Calif. Meets annually, during meeting of Medical Association.

Pennsylvania Radiological Society Secretary, Dr. L. E. Wurster, 416 Pir St. Pa. Next annual meeting, Hershe/H asport, May 17-18, 1940.

PHILADELPHIA ROEN GEN RAY SOCIETY Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from May inclusive, at 8:15 P.M., in Thompson. of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY Secretary, Dr. H. W. ings held second Wedness October to June at vario

ROCHESTER ROENTGEN LAY Secretary, Dr. S. C. Davidsor. an er on second Thursday from 8 P.M., Rochester Academy of Jedicine Build

St. Louis Society of Radiologists
Secretary, Lr. W. K. Mueller, University Meets fourth Wednesday of Octob. James and May, at a place designated by the president.

SAN FRANCISCO RADIOLOGICAL SOCIETY Secretary, Dr. H. A. Hill: 450 Sutter St., S... Francisco.
Meets monthly on third I transday at 7: 5 P.M., first

six mouths at Toland Hall, second six mouths at Lane

Hall.

<sup>\*</sup> Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

SOUTH CAROLINA X-RAY SOCIETY

Secretary, Dr. Hillyer Rudisill, Jr., Roper Hospital, Charleston. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY

Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanocga, Tenn Meets annually at the time and place of the Tennessee State Medical Association.

TEYAS RADIOLOGICAL SOCIETY

Secretary, Dr. L. W. Baird, Scott and White Hospital, Temple, Yexas. Next andual meeting, January 18, 1941,

Sherman, Texas.
University of Michigan Department of Roentgen-

Lees ach Mongay evining Albin C tember to June,

at 7 %. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE Po. E. A Pohle, 1300 University Ave., Madi-Meets they Thursday from 4:00-5:00 P.M., Service Memorial Institute.

ver ver, Va. Meets annually in October.

Vactory, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

Vactory, Pr. I. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday of each month at the College Club, Seattle.

#### CUBA

SCCIEDAD CUBANA DE RADIOLOGIA Y FISIOTERAPIA Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

#### BRITISH EMPIRE

BRITISH INSTITUTE OF RADIOLOGY INCORPORATED WITH THE RÖNTGEN SOCIETY

Meets monthly on third Thursday, from November to June inclusive, at 8:15 p.m., 32 Welbeck St., London. Section of Radiology of the Royal Society of Medi-

CINE (CONFINED TO MEDICAL MEMBERS)

Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, I, Wimpole St., London, W. I.

FACULTY OF RADIOLOGISTS

Or. Barbara M. Key, 32 Welbeck St., London,

ADDOLOGY AND MEDICAL ELECTRICITY, Aus-Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney,

New South Wales.

RADIOLOGICAL SECTION OF THE VICTORIAN BRANCH OF THE B TISH MEDICAL ASSOCIATION

, Dt. Seith Hallam, St. George's Hospital, November inclusive for scientific discussion.

CANADIA A SOCIATION OF RADIOLOGISTS

Sector Singleton, Medical Arts Bldg.,

ADDOLOGY, CANADIAN MEDICAL ASSOCIATION Secr. IF, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S. RADILO YOAL SECT N, NEW ZEALAND BRITISH MEDICAL

\*Dr. Colin Anderson, Invercargill, New Zea-....id. Meets annually.

EUROPE

GENOLOGY Accordes Alliés, 134, Louvain northly on second Sunday at d'Egrace, except in the summertime.

Pal C., except in the summertime.

Secret J. Dr. J. Marce-Crespo, Fuencarral, 7. Madrid,

Spain. Meet one his in Madrid.

Société de Poblo ofie Médicale de France

Meets day on second To sday, except during

months of August and September, 12 Rue de Seine, Paris. GEN-GESELLSCHAFT)

Secretary for French language, Dr. A. Grosjean La Chaux dd Fonds.

Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiol-OGIE MÉDICALE

Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Associate OF CERMAN ROENTGENOLOGISTS AND RADI-CHO-SLOVAKIA
Vidter Altschul, German University, OLOG" S

Secret

Prag . . 52. Beutsche rentgf Gesellschaft (Gesellschaft für RÖNTGENKUNDE UND STRAHLENFORSCHUNG)

Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.

Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

SÜD- UND WESTDEUTSCHE RÖNTGENGESELLSCHAFT

Meets annually in different cities.

NORD- UND OSTDEUTSCHE RÖNTGENGESELLSCHAFT

Meets annually in different cities.

DUTCH SOCIETY OF ELECTROLOGY AND ROENTGENOLOGY Holds two meetings a year in Amsterdam, one in the spring, and one in the fall.

SOCIETA ITALIANA RADIOLOGIA MEDICA

Secretary, M. Ponzio, University of Turin, Prof. Turin SOCIETATEA ROMANA DE RADIOLOGIE SI ELECTROLOGIE Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

ALL-RUSSIAN ROENTGEN RAY ASSOCIATION, LENINGRAD, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.

Secretaries, Drs. S. A. Reinberg and S. G. Simonson.

Meets annually.

LENINGRAD ROENTGEN RAY SOCIETY Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. Ta Konobejevsky. Meets monthly on first Monday at 8 o'clock.

POLISH SOCIETY OF RADIOLOGY Secretary, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology

Secretary, Dr. B. Krynski, 11 Zielna St. Meets once a month except in the summertime. SCANDINAVIAN ROENTGEN SOCIETIES

The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

SOCIETY OF MEDICAL RADIOLOGY IN SWEDEN Meets in Stockholm.

SOCIETY OF MEDICAL RADIOLOGY IN NORWAY. Meets in Oslo.

SOCIETY OF MEDICAL RADIOLOGY IN DENMARK Secretary, Dr. G. Biering, Copenhagen. Meens the second Wednesday of each month from October to July in Copenhagen, at 8 'oclock in the State Institute of Roentgenology.

SOCIETY OF MEDICAL RADIGLOGY IN FINLAND Meets in Helsingfors.

VIENNA ROENTGEN SOCIETY

Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

#### OKIENT

JAPAN X-RAY ASSOCIATION c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

KINKI ROENTGEN-ABEND STEETY
Director, Dr. Prof. Taiga Saire Ogawaoike Tyo Ispan. Meets bi-monthly on third Sunday.

#### BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOG

THE WASHINGTON SCENE

Although the so-called National Health Bill drafted by Senator Wagner last year failed to reach the Senate floor, reports from some sources are that it is currently being revised and will be reintroduced before the Seventy-Sixth Congress adjourns. Meanwhile, various bills intended to accomplish certain aims of the original bill have been introduced in the national Congress.

The Wagner-George Bill, S. 3230, upon which hearings have already been held, called for appropriation of \$10,000,000 the first year for construction of hospitals in needy areas, title to remain in the federal government. The Mead Bill, S. 3246, proposed to authorize a federal appropriation of \$300,000,000 for loans to states for hospitals, water, sewers, stream pollution control, and related projects and facilities. Of the total, \$100,000,000 was to be devoted to hospital projects. Senator Mead, in his bill, defines a hospital as any institution for treating disease, including any health, diagnostic or treatment center, station or clinic.

A bill introduced by Senator Taft of Ohio on April 18 embodies certain of the recommendations contained in a memorandum left by representatives of the American Medical Association following a conference in Washington on January 10. It would provide that the federal government contribute, for a period of five years and from annual appropriations of \$10,000,000, from 40 to 90 per cent of the cost of hospitals constructed with the approval of a National Advisory Hospital Council appointed by the Surgeon-General with the approval of the Federal Security Agency. Title to the hospitals would rest in the local jurisdiction.

In all these bills, equipment to be installed in the hospital is contemplated as a part of the cost of construction, it seems.

In the case of the Wagner-George bill, at least, this would entail a certain amount of governmental supervision in the use of this et aipment. The status of radiologists operating in such hospitals is a matter for conjecture.

Bill was reported out for the Senate Committee on Education and Labor, by Cenator James E. Murray of Montana on April 30. The Committee of Dokking to in its report that the new bill is designed to accomplish part of the original Traject Health Bill and that it is only the initial step in the Committee's projected program.

The revised bill would appropriate \$10,-000,000 the first fiscal year to be used in hospital construction and an equal amount for each of the five succeeding years to be used for grants-in-aid to states and subdivisions thereof for construction and maintenance of hospitals. It also authorizes the use of 2 per cent of the appropriations for the training of personnel necessary for such hospitals. Title can be acquired by the local county or state. The proposal expressly states that the hospitals are to be used for "diagnosis."

Kansas' Senator Capper is less morror in the proposals contained in his bill. Introduced on March 25, it is the revised Epstein Bill and calls for \$50,000,000 the first warrand indeterminate amounts in surgers to induce states to establish of compulsory health insurance up or the Social Security Act.

Senator Henry Cabot Lodge of Massachusetts introduced on March 10 a bill to provide for a Ederal health insurgram and the furnishing of "the services and facilities which have standardized in their nature, but which because of high cost are not direct cases where their use wou and have

In discussing his bill, Senates elin 4, "I believe it is not disputed that a cess instances occur every day in which a revexaminations are desirable—nay, essentiate—but are not given because of the prohibi-

tive cost. The suffering which could be prevented by prompt x-ray examination is indescribable. Needless to say, the prevention of disease automatically tendsurto reduce the cost of caring for the disease once it has been al' to take hold. The use of respirators and x-rays involves a technique which has become relatively standardized. In the case of the x-ray, it is not inconceivable that it would become a routine part sit very physical examination were it not for the cost. In the case of people of/moderate means the cost prohibits its use. In the case of persons who can affordity the use of x-ray is known to be so unusual that its prescription sometimes catises alarm."

A fellow Bostonian, Dr. Hugh Cabot, adds fuel to the flame by continuing his self-appointed rôle of propagandist for medical reform.

Dr. Cabot, it will be recalled, is the author of an article in the April American Mazazine, in which he airs some of his own past practices and concludes that the best way to prohibit the repetition of such ulterior practices as he confesses is to socialize medicine. He is apparently unaware of the national examining boards like the Ameriean Board of Radiology, for he leaves the impression that any doctor may set himset up as a specialist without any special otions. He omits any mention of the fac strenuous efforts are being made by ore nized medicine, without the need for g nental regimentation, to police its own members and raise the standards for specialty practice.

e Journal of the Indiana Medical commenting editorially, "Doctorgets that only a very small per-

cent of M.D.'s are surgeons. Most of the conditions for which patients seek relief are medica functional-not surgical, and one of u. t duties of a octor is to relieve the patient of worry through personal contact. Doctor Cabot is not accustomed to this phase of medical practice—he is used to going to the operating room where the patient is completely ready for the surgery that he performs. He is not called upon to see the patient through the minor difficulties for which the physician collects one and two dollar fees. The big fees of the surgical specialist are best known to him and he has had little opportunity to know about the kind of medical practice that the average physician does-not the extremist or the ultra-conservative, but just the average physician."

> Mac F. Cahal Executive Secretary

### PITTSBURGH ROENTGEN SOCIETY

On Monday, April 29, 1940, the members of the Cleveland Radiological Society were the guests of the Pittsburgh Roentgen Society at a meeting and dinner at the Hotel William Penn in Pittsburgh. Fifty-six members and guests attended and an excellent scientific program was presented. Dr. Lloyd R. Craver of the Memorial Hospital, New York City, spoke on the subject of "Bronchiogenic Carcinoma," Drs. Charles Higley and Harry Hauser of the Cleveland City Hospital spoke on the "Diagnosis and Treatment of Intrathoracic Hodgkin's Disease," and Dr. Paul G. Bovard of Tarentum, Pennsylvania, gave a paper on "Diagnostic Problems Associated with Silicosis."



### DEPARTMENT OF TECHNIQUE

Departr t Editor: Roman Jarr, M.D., B.S., M.A., 105 Rutledge Ave.,

# A SIMPLIFIED GEIGER-MÜLLER COUTE IN TUBE CIRCUIT

By VAN A. ODLE, M.D.\* WASHINGTON, D.C.

SINCE the development of the Geiger-Müller type tube in 1928<sup>1</sup> for the detection of minute quantities of ionizing radiant energy, there have been many improvements in both the tube and associated circuits. Numerous authors have described

Geiger - Muller Tube O Crystal Type ( Headphones 800 Volts + Fig. 1. - 800 Volts + 20 Meg. Ohms Flat Surface 0.5 Mfd. Spark Gan Needle Point munimi +1.5 Volts Steel Vibrator Sprin 4.5 Volts Fig. 2.

circuits for the use of this tube (Locher and Weatherwax; Braestrup, Murphy and Whitaker; Taft, and others).

The circuit described here (Fig. 1) is more simple, compact and portable than any previously described. The successful operation of this circuit depends upon the

fact that crystal type headphones and the high impedance of this type of headphone enables it to be connected in series with the high impedance of the Geiger-Müller tube, and a very satisfact by response is obtained without auditional amplification. It is obvious that the circuit is designed for use with headphones only. In many applications of the Geiger-Müller tube this is all that is desired as in the finding of lost radium, etc.

ar it is year compac

It is desirable to have a portable power supply for use with the above described circuit. There are small portable batteries designed especially for use in stratosphere balloons. These batteries would probably be an ideal high voltage source but have not been commonly used due to their cost. A portable high voltage power supply has been described by Taft, which oper esupon the same principle as the upply of an automobile radic the uses an induction coil and very a tube rectifier.

The power supply used by operates upon the same principal the one noted above but has been neral respects in regard to derate interrupter and transformer. This produces greater stability voltage circuit. Due to the the voltage in the seconds may be used as a rectifier very efficient in this case, thus may be used as a rectifier very efficient in this case, thus may be some of this spark gap should be a needle point and the other side a flat surface as shown in the diagram. The detector

<sup>\*</sup> Fellow in Radiology with Drs. Groover, Christie and Merritt at Georgetown University Hospital and Medical School, Washington, D. C.

circuit must be shielded from the power supply circuit. In the circuits as described above there is no audible power supply to the circuits as described above there is no audible power supply to the circuits as described and Müller, W. Phys. Ztschr., noise produced in the headphones. The release terms, ground symbol as used in the diagrams refers to the metal cabinet as being at ground potential wan respect to the re-

The ain features of this instrument are the very apact, simple and readily postable. The envire apparatus, with the exce, ion of the neadphones, is contained in a metal cabinet  $6 \times 6 \times 6$  inches.

## REFERENCES

Geiger-Müller counters for locating radium and for measuring gamma-ra; intensities. Radi-

ology, 1936, 27, 145-157.

3. Braestrup, C. B. Aurphy, E. J., and Whitaker, M. D. Radiological applications of the Geiger-Müller counter. Am. J. ROENTGENOL. & RAD. THERAPY, 1937, 38, 915-922.

4. TAFT, R. B., Battery operated Geiger-Müller counters with a new type of voltage supply. Radiology, 1936, 27, 616-617.



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